Package 'epiR'

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Title Tools for the Analysis of Epidemiological Data

Author Mark Stevenson <mark.stevenson1@unimelb.edu.au> with contributions from Telmo Nunes, Cord Heuer, Jonathon Marshall, Javier Sanchez, Ron Thornton, Jeno Reiczigel, Jim Robison-Cox, Paola Sebastiani, Peter Solymos, Kazuki Yoshida, Geoff Jones, Sarah Pirikahu, Simon Firestone, Ryan Kyle, Johann Popp and Mathew Jay.

Maintainer Mark Stevenson <mark.stevenson1@unimelb.edu.au>

Description Tools for the analysis of epidemiological data. Contains functions for directly and indirectly adjusting measures of disease frequency, quantifying measures of association on the basis of single or multiple strata of count data presented in a contingency table, and computing confidence intervals around incidence risk and incidence rate estimates. Miscellaneous functions for use in meta-analysis, diagnostic test interpretation, and sample size calculations.

Depends R (>= 3.0.0), survival

Imports BiasedUrn, methods

Suggests MASS (>= 3.1-20)

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R topics documented:

`epi.2by2` *Summary measures for count data presented in a 2 by 2 table*

Description

Computes summary measures of risk and a chi-squared test for difference in the observed proportions from count data presented in a 2 by 2 table. With multiple strata the function returns crude and Mantel-Haenszel adjusted measures of association and chi-squared tests of homogeneity.

Usage

```
epi.2by2(dat, method = "cohort.count", conf.level = 0.95, units = 100,
   homogeneity = "breslow.day", outcome = "as.columns")

## S3 method for class 'epi.2by2'
print(x, ...)

## S3 method for class 'epi.2by2'
summary(object, ...)
```

Arguments

`dat`	an object of class `table` containing the individual cell frequencies. See the examples, below, for details.
`method`	a character string indicating the study design on which the tabular data has been based. Options are `cohort.count`, `cohort.time`, `case.control`, or `cross.sectional`. Based on the study design specified by the user, appropriate measures of association, measures of effect in the exposed and measures of effect in the population are returned by the function.
`conf.level`	magnitude of the returned confidence intervals. Must be a single number between 0 and 1.
`units`	multiplier for prevalence and incidence (risk or rate) estimates.
`homogeneity`	a character string indicating the type of homogeneity test to perform. Options are `breslow.day` or `woolf`.
`outcome`	a character string indicating how the outcome variable is represented in the contingency table. Options are `as.columns` (outcome as columns) or `as.rows` (outcome as rows).
`x, object`	an object of class `epi.2by2`.
`...`	Ignored.

Details

Where method is `cohort.count`, `case.control`, or `cross.sectional` and `outcome = as.columns` the required 2 by 2 table format is:

	Disease +	Disease -	Total
Expose +	a	b	a+b
Expose -	c	d	c+d
Total	a+c	b+d	a+b+c+d

Where method is `cohort.time` and `outcome = as.columns` the required 2 by 2 table format is:

	Disease +	Time at risk
Expose +	a	b
Expose -	c	d
Total	a+c	b+d

A summary of the methods used for each of the confidence interval calculations in this function is as follows:

Value

An object of class `epi.2by2` comprised of:

`method`	character string returning the study design specified by the user.
`n.strata`	number of strata.
`conf.level`	magnitude of the returned confidence intervals.
`massoc`	a list comprised of the computed measures of association, measures of effect in the exposed and measures of effect in the population. See below for details.
`tab`	a data frame comprised of of the contingency table data.

When method equals `cohort.count` the following measures of association, measures of effect in the exposed and measures of effect in the population are returned:

`RR`	Wald and score confidence intervals for the incidence risk ratios for each strata. Wald and score confidence intervals for the crude incidence risk ratio. Wald confidence interval for the Mantel-Haenszel adjusted incidence risk ratio.
`OR`	Wald, score, Cornfield and maximum likelihood confidence intervals for the odds ratios for each strata. Wald, score, Cornfield and maximum likelihood confidence intervals for the crude odds ratio. Wald confidence interval for the Mantel-Haenszel adjusted odds ratio.

ARisk	Wald and score confidence intervals for the attributable risk (risk difference) for each strata. Wald and score confidence intervals for the crude attributable risk. Wald, Sato and Greenland-Robins confidence intervals for the Mantel-Haenszel adjusted attributable risk.
PARisk	Wald and Pirikahu confidence intervals for the population attributable risk for each strata. Wald and Pirikahu confidence intervals for the crude population attributable risk. The Pirikahu confidence intervals are calculated using the delta method.
AFRisk	Wald confidence intervals for the attributable fraction for each strata. Wald confidence intervals for the crude attributable fraction.
PAFRisk	Wald confidence intervals for the population attributable fraction for each strata. Wald confidence intervals for the crude population attributable fraction.
chisq.strata	chi-squared test for difference in exposed and non-exposed proportions for each strata.
chisq.crude	chi-squared test for difference in exposed and non-exposed proportions across all strata.
chisq.mh	Mantel-Haenszel chi-squared test.
RR.homog	test of homogeneity of the individual strata incidence risk ratios.
OR.homog	test of homogeneity of the individual strata odds ratios.

When method equals cohort.time the following measures of association and effect are returned:

IRR	Wald confidence interval for the incidence rate ratios for each strata. Wald confidence interval for the crude incidence rate ratio. Wald confidence interval for the Mantel-Haenszel adjusted incidence rate ratio.
ARate	Wald confidence interval for the attributable rate for each strata. Wald confidence interval for the crude attributable rate. Wald confidence interval for the Mantel-Haenszel adjusted attributable rate.
PARate	Wald confidence interval for the population attributable rate for each strata. Wald confidence intervals for the crude population attributable rate.
AFRate	Wald confidence interval for the attributable fraction for each strata. Wald confidence interval for the crude attributable fraction.
PAFRate	Wald confidence interval for the population attributable fraction for each strata. Wald confidence interval for the crude poulation attributable fraction.
chisq.strata	chi-squared test for difference in exposed and non-exposed proportions for each strata.
chisq.crude	chi-squared test for difference in exposed and non-exposed proportions across all strata.
chisq.mh	Mantel-Haenszel chi-squared test.

When method equals case.control the following measures of association and effect are returned:

OR	Wald, score, Cornfield and maximum likelihood confidence intervals for the odds ratios for each strata. Wald, score, Cornfield and maximum likelihood confidence intervals for the crude odds ratio. Wald confidence interval for the Mantel-Haenszel adjusted odds ratio.

ARisk	Wald and score confidence intervals for the attributable risk for each strata. Wald and score confidence intervals for the crude attributable risk. Wald, Sato and Greenland-Robins confidence intervals for the Mantel-Haenszel adjusted attributable risk.
PARisk	Wald and Pirikahu confidence intervals for the population attributable risk for each strata. Wald and Pirikahu confidence intervals for the crude population attributable risk.
AFest	Wald confidence intervals for the estimated attributable fraction for each strata. Wald confidence intervals for the crude estimated attributable fraction.
PAFest	Wald confidence intervals for the population estimated attributable fraction for each strata. Wald confidence intervals for the crude population estimated attributable fraction.
chisq.strata	chi-squared test for difference in exposed and non-exposed proportions for each strata.
chisq.crude	chi-squared test for difference in exposed and non-exposed proportions across all strata.
chisq.mh	Mantel-Haenszel chi-squared test.
OR.homog	test of homogeneity of the individual strata odds ratios.

When method equals `cross.sectional` the following measures of association and effect are returned:

PR	Wald and score confidence intervals for the prevalence ratios for each strata. Wald and score confidence intervals for the crude prevalence ratio. Wald confidence interval for the Mantel-Haenszel adjusted prevalence ratio.
OR	Wald, score, Cornfield and maximum likelihood confidence intervals for the odds ratios for each strata. Wald, score, Cornfield and maximum likelihood confidence intervals for the crude odds ratio. Wald confidence interval for the Mantel-Haenszel adjusted odds ratio.
ARisk	Wald and score confidence intervals for the attributable risk for each strata. Wald and score confidence intervals for the crude attributable risk. Wald, Sato and Greenland-Robins confidence intervals for the Mantel-Haenszel adjusted attributable risk.
PARisk	Wald and Pirikahu confidence intervals for the population attributable risk for each strata. Wald and Pirikahu confidence intervals for the crude population attributable risk.
AFRisk	Wald confidence intervals for the attributable fraction for each strata. Wald confidence intervals for the crude attributable fraction.
PAFRisk	Wald confidence intervals for the population attributable fraction for each strata. Wald confidence intervals for the crude population attributable fraction.
chisq.strata	chi-squared test for difference in exposed and non-exposed proportions for each strata.
chisq.crude	chi-squared test for difference in exposed and non-exposed proportions across all strata.

chisq.mh	Mantel-Haenszel chi-squared test.
PR.homog	test of homogeneity of the individual strata prevalence ratios.
OR.homog	test of homogeneity of the individual strata odds ratios.

The point estimates of the wald, score and cfield odds ratios are calculated using the cross product method. Method mle computes the conditional maximum likelihood estimate of the odds ratio.

Note

Measures of association include the prevalence ratio, the incidence risk ratio, the incidence rate ratio and the odds ratio. The incidence risk ratio is the ratio of the incidence risk of disease in the exposed group to the incidence risk of disease in the unexposed group. The odds ratio (also known as the cross-product ratio) is an estimate of the incidence risk ratio. When the incidence of an outcome in the study population is low (say, less than 5%) the odds ratio will provide a reliable estimate of the incidence risk ratio. The more frequent the outcome becomes, the more the odds ratio will overestimate the incidence risk ratio when it is greater than than 1 or understimate the incidence risk ratio when it is less than 1.

Measures of effect in the exposed include the attributable risk (or prevalence) and the attributable fraction. The attributable risk is the risk of disease in the exposed group minus the risk of disease in the unexposed group. The attributable risk provides a measure of the absolute increase or decrease in risk associated with exposure. The attributable fraction is the proportion of study outcomes in the exposed group that is attributable to exposure.

Measures of effect in the population include the population attributable risk (or prevalence) and the population attributable fraction (also known as the aetiologic fraction). The population attributable risk is the risk of the study outcome in the population that may be attributed to exposure. The population attributable fraction is the proportion of the study outcomes in the population that is attributable to exposure.

Point estimates and confidence intervals for the prevalence ratio and incidence risk ratio are calculated using Wald (Wald 1943) and score methods (Miettinen and Nurminen 1985). Point estimates and confidence intervals for the incidence rate ratio are calculated using the exact method described by Kirkwood and Sterne (2003) and Juul (2004). Point estimates and confidence intervals the odds ratio are calculated using Wald (Wald 1943), score (Miettinen and Nurminen 1985) and maximum likelihood methods (Fleiss et al. 2003). Point estimates and confidence intervals for the population attributable risk are calculated using formulae provided by Rothman and Greenland (1998, p 271) and Pirikahu (2014). Point estimates and confidence intervals for the population attributable fraction are calculated using formulae provided by Jewell (2004, p 84 - 85). Point estimates and confidence intervals for the Mantel-Haenszel adjusted attributable risk are calculated using formulae provided by Klingenberg (2014).

Wald confidence intervals are provided in the summary table simply because they are widely used and would be familiar to most users.

The Mantel-Haenszel adjusted measures of association are valid when the measures of association across the different strata are similar (homogenous), that is when the test of homogeneity of the odds (risk) ratios is not significant.

The tests of homogeneity of the odds (risk) ratio where homogeneity = "breslow.day" and homogeneity = "woolf" are based on Jewell (2004, p 152 - 158). Thanks to Jim Robison-Cox for sharing his implementation of these functions.

Author(s)

Mark Stevenson (Faculty of Veterinary and Agricultural Sciences, The University of Melbourne, Australia), Cord Heuer (EpiCentre, IVABS, Massey University, Palmerston North, New Zealand), Jim Robison-Cox (Department of Math Sciences, Montana State University, Montana, USA), Kazuki Yoshida (Brigham and Women's Hospital, Boston Massachusetts, USA) and Simon Firestone (Faculty of Veterinary and Agricultural Sciences, The University of Melbourne, Australia). Thanks to Ian Dohoo for numerous helpful suggestions to improve the documentation for this function.

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Examples

```
## EXAMPLE 1:
## A cross sectional study investigating the relationship between dry cat
## food (DCF) and feline urologic syndrome (FUS) was conducted (Willeberg
## 1977). Counts of individuals in each group were as follows:

## DCF-exposed cats (cases, non-cases) 13, 2163
## Non DCF-exposed cats (cases, non-cases) 5, 3349

## Outcome variable (FUS) as columns:
dat <- matrix(c(13,2163,5,3349), nrow = 2, byrow = TRUE)
rownames(dat) <- c("DF+", "DF-"); colnames(dat) <- c("FUS+", "FUS-"); dat

epi.2by2(dat = as.table(dat), method = "cross.sectional",
   conf.level = 0.95, units = 100,  homogeneity = "breslow.day",
   outcome = "as.columns")

## Outcome variable (FUS) as rows:
dat <- matrix(c(13,5,2163,3349), nrow = 2, byrow = TRUE)
rownames(dat) <- c("FUS+", "FUS-"); colnames(dat) <- c("DF+", "DF-"); dat

epi.2by2(dat =  as.table(dat), method = "cross.sectional",
   conf.level = 0.95, units = 100,  homogeneity = "breslow.day",
   outcome = "as.rows")

## Prevalence ratio:
## The prevalence of FUS in DCF exposed cats is 4.01 (95% CI 1.43 to 11.23)
## times greater than the prevalence of FUS in non-DCF exposed cats.
```

```
## Attributable fraction in the exposed:
## In DCF exposed cats, 75% of FUS is attributable to DCF (95% CI 30% to
## 91%).

## Attributable fraction in the population:
## Fifty-four percent of FUS cases in the cat population are attributable
## to DCF (95% CI 4% to 78%).

## EXAMPLE 2:
## This example shows how the table function can be used to pass data to
## epi.2by2. Here we use the birthwgt data from the MASS package.

library(MASS)
dat1 <- birthwt; head(dat1)

## Generate a table of cell frequencies. First set the levels of the outcome
## and the exposure so the frequencies in the 2 by 2 table come out in the
## conventional format:
dat1$low <- factor(dat1$low, levels = c(1,0))
dat1$smoke <- factor(dat1$smoke, levels = c(1,0))
dat1$race <- factor(dat1$race, levels = c(1,2,3))

## Generate the 2 by 2 table. Exposure (rows) = smoke. Outcome (columns) = low.
tab1 <- table(dat1$smoke, dat1$low, dnn = c("Smoke", "Low BW"))
print(tab1)

## Compute the incidence risk ratio and other measures of association:
epi.2by2(dat = tab1, method = "cohort.count",
   conf.level = 0.95, units = 100,  homogeneity = "breslow.day",
   outcome = "as.columns")

## Odds ratio:
## The odds of having a low birth weight child for smokers is 2.02
## (95% CI 1.08 to 3.78) times  greater than the odds of having
## a low birth weight child for non-smokers.

## Now stratify by race:
tab2 <- table(dat1$smoke, dat1$low, dat1$race,
   dnn = c("Smoke", "Low BW", "Race"))
print(tab2)

## Compute the crude odds ratio, the Mantel-Haenszel adjusted odds ratio
## and other measures of association:
rval <- epi.2by2(dat = tab2, method = "cohort.count",
   conf.level = 0.95, units = 100,  homogeneity = "breslow.day",
   outcome = "as.columns")
print(rval)

## After accounting for the confounding effect of race, the odds of
## having a low birth weight child for smokers is 3.09 (95% CI 1.49 to 6.39)
## times that of non-smokers.
```

```
## Compare the Greenland-Robins confidence intervals for the Mantel-Haenszel
## adjusted attributable risk with the Wald confidence intervals for the
## Mantel-Haenszel adjusted attributable risk:

rval$massoc$ARisk.mh.green
rval$massoc$ARisk.mh.wald

## Now turn tab2 into a data frame where the frequencies of individuals in
## each exposure-outcome category are provided. Often your data will be
## presented in this summary format:
dat2 <- data.frame(tab2)
print(dat2)

## Re-format dat2 (a summary count data frame) into tabular format using the
## xtabs function:
tab3 <- xtabs(Freq ~ Smoke + Low.BW + Race, data = dat2)
print(tab3)

# tab3 can now be passed to epi.2by2:
rval <- epi.2by2(dat = tab3, method = "cohort.count",
   conf.level = 0.95, units = 100,  homogeneity = "breslow.day",
   outcome = "as.columns")
print(rval)

## The Mantel-Haenszel adjusted odds ratio is 3.09 (95% CI 1.49 to 6.39). The
## ratio of the crude odds ratio to the Mantel-Haensel adjusted odds ratio is
## 0.66.

## What are the Cornfield confidence limits, the maximum likelihood
## confidence limits and the score confidence limits for the crude odds ratio?
rval$massoc$OR.crude.cfield
rval$massoc$OR.crude.mle
rval$massoc$OR.crude.score

## Cornfield: 2.02 (95% CI 1.07 to 3.79)
## Maximum likelihood: 2.01 (1.03 to 3.96)
# Score: 2.02 (95% CI 1.08 to 3.77)

## Plot the individual strata-level odds ratios and compare them with the
## Mantel-Haenszel adjusted odds ratio.

## Not run:
library(ggplot2); library(scales)

nstrata <- 1:dim(tab3)[3]
strata.lab <- paste("Strata ", nstrata, sep = "")
y.at <- c(nstrata, max(nstrata) + 1)
y.lab <- c("M-H", strata.lab)
x.at <- c(0.25, 0.5, 1, 2, 4, 8, 16, 32)

or.l <- c(rval$massoc$OR.mh$lower, rval$massoc$OR.strata.cfield$lower)
or.u <- c(rval$massoc$OR.mh$upper, rval$massoc$OR.strata.cfield$upper)
or.p <- c(rval$massoc$OR.mh$est, rval$massoc$OR.strata.cfield$est)
```

```
dat <- data.frame(y.at, y.lab, or.p, or.l, or.u)

ggplot(dat, aes(or.p, y.at)) +
   geom_point() +
   geom_errorbarh(aes(xmax = or.l, xmin = or.u, height = 0.2)) +
   labs(x = "Odds ratio", y = "Strata") +
   scale_x_continuous(trans = log2_trans(), breaks = x.at,
   limits = c(0.25,32)) + scale_y_continuous(breaks = y.at, labels = y.lab) +
   geom_vline(xintercept = 1, lwd = 1) + coord_fixed(ratio = 0.75 / 1) +
   theme(axis.title.y = element_text(vjust = 0))

## End(Not run)

## EXAMPLE 3:
## A study was conducted by Feychting et al (1998) comparing cancer occurrence
## among the blind with occurrence among those who were not blind but had
## severe visual impairment. From these data we calculate a cancer rate of
## 136/22050 person-years among the blind compared with 1709/127650 person-
## years among those who were visually impaired but not blind.

## Not run:
dat <- as.table(matrix(c(136,22050,1709,127650), nrow = 2, byrow = TRUE))
rval <- epi.2by2(dat = dat, method = "cohort.time", conf.level = 0.95,
   units = 1000,  homogeneity = "breslow.day", outcome = "as.columns")
summary(rval)$ARate.strata.wald

## The incidence rate of cancer was 7.22 cases per 1000 person-years less in the
## blind, compared with those who were not blind but had severe visual impairment
## (90% CI 6.00 to 8.43 cases per 1000 person-years).

round(summary(rval)$IRR.strata.wald, digits = 2)

## End(Not run)

## The incidence rate of cancer in the blind group was less than half that of the
## comparison group (incidence rate ratio 0.46, 90% CI 0.38 to 0.55).

## EXAMPLE 4:
## A study has been conducted to assess the effect of a new treatment for
## mastitis in dairy cows. Eight herds took part in the study. The following
## data were obtained. The vectors ai, bi, ci and di list (for each herd) the
## number of cows in the E+D+, E+D-, E-D+ and E-D- groups, respectively.

## Not run:
hid <- 1:8
ai <- c(23,10,20,5,14,6,10,3)
bi <- c(10,2,1,2,2,2,3,0)
ci <- c(3,2,3,2,1,3,3,2)
di <- c(6,4,3,2,6,3,1,1)
dat <- data.frame(hid, ai, bi, ci, di)
print(dat)

## Re-format data frame dat into a format suitable for epi.2by2:
```

```
hid <- rep(1:8, times = 4)
exp <- factor(rep(c(1,1,0,0), each = 8), levels = c(1,0))
out <- factor(rep(c(1,0,1,0), each = 8), levels = c(1,0))
dat <- data.frame(hid, exp, out, n = c(ai,bi,ci,di))
dat <- xtabs(n ~ exp + out + hid, data = dat)
print(dat)

epi.2by2(dat = dat, method = "cohort.count", homogeneity = "breslow.day",
   outcome= "as.columns")

## After adjusting for the effect of herd, compared to untreated cows, treatment
## increased the odds of recovery by a factor of 5.97 (95% CI 2.72 to 13.13).

## End(Not run)
```

`epi.about` *The library epiR: summary information*

Description

Tools for the analysis of epidemiological data.

Usage

```
epi.about()
```

Details

The most recent version of the epiR package can be obtained from: http://fvas.unimelb.edu.au/veam

Author(s)

Mark Stevenson (<mark.stevenson1@unimelb.edu.au>), Faculty of Veterinary and Agricultural Sciences, University of Melbourne, Parkville, Victoria 3010, Australia.

Simon Firestone, Faculty of Veterinary and Agricultural Sciences, University of Melbourne, Parkville, Victoria 3010, Australia.

Telmo Nunes, UISEE/DETSA, Faculdade de Medicina Veterinaria — UTL, Rua Prof. Cid dos Santos, 1300 - 477 Lisboa Portugal.

Javier Sanchez, Atlantic Veterinary College, University of Prince Edward Island, Charlottetown, Prince Edward Island, C1A 4P3, Canada.

Ron Thornton, Ministry for Primary Industries New Zealand, PO Box 2526 Wellington, New Zealand.

epi.asc *Write matrix to an ASCII raster file*

Description

Writes a data frame to an ASCII raster file, suitable for display in a Geographic Information System.

Usage

```
epi.asc(dat, file, xllcorner, yllcorner, cellsize, na = -9999)
```

Arguments

dat	a matrix with data suitable for plotting using the image function.
file	character string specifying the name and path of the ASCII raster output file.
xllcorner	the easting coordinate corresponding to the lower left hand corner of the matrix.
yllcorner	the northing coordinate corresponding to the lower left hand corner of the matrix.
cellsize	number, defining the size of each matrix cell.
na	scalar, defines null values in the matrix. NAs are converted to this value.

Value

Writes an ASCII raster file (typically with *.asc extension), suitable for display in a Geographic Information System.

Note

The image function in R rotates tabular data counter clockwise by 90 degrees for display. A matrix of the form:

1 3
2 4

is displayed (using image) as:

3 4
1 2

It is recommended that the source data for this function is a matrix. Replacement of NAs in a data frame extends processing time for this function.

epi.betabuster *An R version of Wes Johnson and Chun-Lung Su's Betabuster*

Description

A function to return shape1 and shape2 parameters for a beta distribution, based on expert elicitation.

Usage

```
epi.betabuster(mode, conf, greaterthan, x, conf.level = 0.95, max.shape1 = 100,
   step = 0.001)
```

Arguments

mode	scalar, the mode of the variable of interest. Must be a number between 0 and 1.
conf	level of confidence (expressed on a 0 to 1 scale) that the true value of the variable of interest is greater or less than argument x.
greaterthan	logical, if TRUE you are making the statement that you are conf confident that the true value of the variable of interest is greater than x. If FALSE you are making the statement that you are conf confident that the true value of the variable of interest is less than x.
x	scalar, value of the variable of interest (see above).
conf.level	magnitude of the returned confidence interval for the estimated beta distribution. Must be a single number between 0 and 1.
max.shape1	scalar, maximum value of the shape1 parameter for the beta distribution.
step	scalar, step value for the shape1 parameter. See details.

Details

The beta distribution has two parameters: shape1 and shape2, corresponding to a and b in the original verion of BetaBuster. If r equals the number of times an event has occurred after n trials, shape1 = (r + 1) and shape2 = (n - r + 1).

BetaBuster can be downloaded from http://www.ics.uci.edu/~wjohnson/BIDA/betabuster.zip.

Value

A list containing the following:

shape1	the shape1 parameter for the estimated beta distribution.
shape2	the shape2 parameter for the estimated beta distribution.
mode	the mode of the estimated beta distribution.
mean	the mean of the estimated beta distribution.

median	the median of the estimated beta distribution.
lower	the lower bound of the confidence interval of the estimated beta distribution.
upper	the upper bound of the confidence interval of the estimated beta distribution.
variance	the variance of the estimated beta distribution.

Author(s)

Simon Firestone (Faculty of Veterinary and Agricultural Sciences, The University of Melbourne, Australia) with acknowledgements to Wes Johnson and Chun-Lung Su for the original standalone software.

References

Christensen R, Johnson W, Branscum A, Hanson TE (2010). Bayesian Ideas and Data Analysis: An Introduction for Scientists and Statisticians. Chapman and Hall, Boca Raton.

Examples

```
## EXAMPLE 1:
## If a scientist is asked for their best guess for the diagnostic sensitivity
## of a particular test and the answer is 0.90, and if they are also willing
## to assert that they are 80% certain that the sensitivity is greater than
## 0.75, what are the shape1 and shape2 parameters for a beta distribution
## satisfying these constraints?

rval <- epi.betabuster(mode = 0.90, conf = 0.80, greaterthan = TRUE,
   x = 0.75, conf.level = 0.95, max.shape1 = 100, step = 0.001)
rval$shape1; rval$shape2

## The shape1 and shape2 parameters for the beta distribution that satisfy the
## constraints listed above are 9.875 and 1.986, respectively.

## This beta distribution reflects the probability distribution
## obtained if there were 9 successes, r:
r <- rval$shape1 - 1; r

## from 10 trials, n:
n <- rval$shape2 + rval$shape1 - 2; n

dat <- data.frame(x = seq(from = 0, to = 1, by = 0.001),
   y = dbeta(x = seq(from = 0, to = 1,by = 0.001),
   shape1 = rval$shape1, shape2 = rval$shape2))

## Density plot of the estimated beta distribution:

## Not run:
library(ggplot2)

windows(); ggplot(data = dat, aes(x = x, y = y)) +
   geom_line() +
   xlab("Test sensitivity") +
```

```
    ylab("Density")

## End(Not run)
```

---

epi.bohning *Bohning's test for overdispersion of Poisson data*

Description

A test for overdispersion of Poisson data.

Usage

```
epi.bohning(obs, exp, alpha = 0.05)
```

Arguments

obs	the observed number of cases in each area.
exp	the expected number of cases in each area.
alpha	alpha level to be used for the test of significance. Must be a single number between 0 and 1.

Value

A data frame with two elements: `test.statistic`, Bohning's test statistic and `p.value` the associated P-value.

References

Bohning D (2000). Computer-assisted Analysis of Mixtures and Applications. Chapman and Hall, Boca Raton.

Ugarte MD, Ibanez B, Militino AF (2006). Modelling risks in disease mapping. Statistical Methods in Medical Research 15: 21 - 35.

Examples

```
data(epi.SClip)
obs <- epi.SClip$cases
pop <- epi.SClip$population
exp <- (sum(obs) / sum(pop)) * pop

epi.bohning(obs, exp, alpha = 0.05)
```

epi.ccc *Concordance correlation coefficient*

Description

Calculates Lin's (1989, 2000) concordance correlation coefficient for agreement on a continuous measure.

Usage

```
epi.ccc(x, y, ci = "z-transform", conf.level = 0.95, rep.measure = FALSE,
   subjectid)
```

Arguments

x	a vector, representing the first set of measurements.
y	a vector, representing the second set of measurements.
ci	a character string, indicating the method to be used. Options are z-transform or asymptotic.
conf.level	magnitude of the returned confidence interval. Must be a single number between 0 and 1.
rep.measure	logical. If TRUE there are repeated observations across subject.
subjectid	a factor providing details of the observer identifier if rep.measure == TRUE.

Details

Computes Lin's (1989, 2000) concordance correlation coefficient for agreement on a continuous measure obtained by two methods. The concordance correlation coefficient combines measures of both precision and accuracy to determine how far the observed data deviate from the line of perfect concordance (that is, the line at 45 degrees on a square scatter plot). Lin's coefficient increases in value as a function of the nearness of the data's reduced major axis to the line of perfect concordance (the accuracy of the data) and of the tightness of the data about its reduced major axis (the precision of the data).

Both x and y values need to be present for a measurement pair to be included in the analysis. If either or both values are missing (i.e. coded NA) then the measurement pair is deleted before analysis.

Value

A list containing the following:

rho.c	the concordance correlation coefficient.
s.shift	the scale shift.
l.shift	the location shift.
C.b	a bias correction factor that measures how far the best-fit line deviates from a line at 45 degrees. No deviation from the 45 degree line occurs when C.b = 1. See Lin (1989, page 258).

blalt	a data frame with two columns: mean the mean of each pair of measurements, delta vector y minus vector x.
sblalt	a data frame listing the average difference between the two sets of measurements, the standard deviation of the difference between the two sets of measurements and the lower and upper confidence limits of the difference between the two sets of measurements. If rep.measure == TRUE the confidence interval of the difference is adjusted to account for repeated observations across individual subjects.
nmissing	a count of the number of measurement pairs ignored due to missingness.

References

Bland J, Altman D (1986). Statistical methods for assessing agreement between two methods of clinical measurement. The Lancet 327: 307 - 310.

Bland J, Altman D (1999). Measuring agreement in method comparison studies. Statistical Methods in Medical Research 8: 135 - 160.

Bland J, Altman D (2007). Agreement between methods of measurement with multiple observations per individual. Journal of Biopharmaceutical Statistics 17: 571 - 582. (Corrects the formula quoted in the 1999 paper).

Bradley E, Blackwood L (1989). Comparing paired data: a simultaneous test for means and variances. American Statistician 43: 234 - 235.

Burdick RK, Graybill FA (1992). Confidence Intervals on Variance Components. New York: Dekker.

Dunn G (2004). Statistical Evaluation of Measurement Errors: Design and Analysis of Reliability Studies. London: Arnold.

Euser AM, Dekker FW, le Cessie S (2008). A practical approach to Bland-Altman plots and variation coefficients for log transformed variables. Journal of Clinical Epidemiology 61: 978 - 982.

Hsu C (1940). On samples from a normal bivariate population. Annals of Mathematical Statistics 11: 410 - 426.

Krippendorff K (1970). Bivariate agreement coefficients for reliability of data. In: Borgatta E, Bohrnstedt G (eds) Sociological Methodology. San Francisco: Jossey-Bass, pp. 139 - 150.

Lin L (1989). A concordance correlation coefficient to evaluate reproducibility. Biometrics 45: 255 - 268.

Lin L (2000). A note on the concordance correlation coefficient. Biometrics 56: 324 - 325.

Pitman E (1939). A note on normal correlation. Biometrika 31: 9 - 12.

Reynolds M, Gregoire T (1991). Comment on Bradley and Blackwood. American Statistician 45: 163 - 164.

Snedecor G, Cochran W (1989). Statistical Methods. Ames: Iowa State University Press.

See Also

epi.occc

Examples

```
## EXAMPLE 1:
set.seed(seed = 1234)
method1 <- rnorm(n = 100, mean = 0, sd = 1)
method2 <- method1 + runif(n = 100, min = -0.25, max = 0.25)

## Add some missing values:
method1[50] <- NA
method2[75] <- NA

tmp <- data.frame(method1, method2)
tmp.ccc <- epi.ccc(method1, method2, ci = "z-transform", conf.level = 0.95,
   rep.measure = FALSE)

tmp.lab <- data.frame(lab = paste("CCC: ",
   round(tmp.ccc$rho.c[,1], digits = 2), " (95% CI ",
   round(tmp.ccc$rho.c[,2], digits = 2), " - ",
   round(tmp.ccc$rho.c[,3], digits = 2), ")", sep = ""))

z <- lm(method2 ~ method1)
alpha <- summary(z)$coefficients[1,1]
beta <-  summary(z)$coefficients[2,1]
tmp.lm <- data.frame(alpha, beta)

## Concordance correlation plot:
## Not run:
library(ggplot2)

ggplot(tmp, aes(x = method1, y = method2)) +
   geom_point() +
   geom_abline(intercept = 0, slope = 1) +
   geom_abline(data = tmp.lm, aes(intercept = alpha, slope = beta),
      linetype = "dashed") +
   xlim(0, 3) +
   ylim(0, 3) +
   xlab("Method 1") +
   ylab("Method 2") +
   geom_text(data = tmp.lab, x = 0.5, y = 2.95, label = tmp.lab$lab) +
   coord_fixed(ratio = 1 / 1)

## In this plot the dashed line represents the line of perfect concordance.
## The solid line represents the reduced major axis.

## End(Not run)


## EXAMPLE 2:
## Bland and Altman plot (Figure 2 from Bland and Altman 1986):
x <- c(494,395,516,434,476,557,413,442,650,433,417,656,267,
   478,178,423,427)
```

```
y <- c(512,430,520,428,500,600,364,380,658,445,432,626,260,
   477,259,350,451)

tmp.ccc <- epi.ccc(x, y, ci = "z-transform", conf.level = 0.95,
   rep.measure = FALSE)
tmp <- data.frame(mean = tmp.ccc$blalt[,1], delta = tmp.ccc$blalt[,2])

## Not run:
library(ggplot2)

ggplot(tmp.ccc$blalt, aes(x = mean, y = delta)) +
  geom_point() +
  geom_hline(data = tmp.ccc$sblalt, aes(yintercept = lower), linetype = 2) +
  geom_hline(data = tmp.ccc$sblalt, aes(yintercept = upper), linetype = 2) +
  geom_hline(data = tmp.ccc$sblalt, aes(yintercept = est), linetype = 1) +
  xlab("Average PEFR by two meters (L/min)") +
  ylab("Difference in PEFR (L/min)") +
  xlim(0,800) +
  ylim(-150,150)

## End(Not run)


## EXAMPLE 3:
## Setting limits of agreement when your data are skewed. See Euser et al.
## (2008) for details.
x <- c(0,210,15,90,0,0,15,0,0,0,15,0,15,0,0,0,0,15,0,0,15,135,0,0,15,
   120,30,15,30,0,0,5235,780,1275,10515,1635,1905,1830,720,450,225,420,
   300,15,285,0,225,525,675,5280,465,270,0,1485,15,420,0,60,0,0,0,750,
   570,0)
y <- c(0,70,0,0,0,0,35,0,0,0,0,0,0,35,0,0,0,0,0,0,35,35,70,0,0,140,35,
   105,0,0,0,1190,385,1190,6930,560,1260,700,840,0,105,385,245,35,105,
   0,140,350,350,3640,385,350,0,1505,0,630,70,0,0,140,0,420,490,0)

crude.ccc <- epi.ccc(x, y, ci = "z-transform",
   conf.level = 0.95, rep.measure = FALSE)

## Not run:
library(ggplot2)

ggplot(crude.ccc$blalt, aes(x = mean, y = delta)) +
  geom_point() +
  geom_hline(data = crude.ccc$sblalt, aes(yintercept = lower), linetype = 2) +
  geom_hline(data = crude.ccc$sblalt, aes(yintercept = upper), linetype = 2) +
  geom_hline(data = crude.ccc$sblalt, aes(yintercept = est), linetype = 1) +
  xlab("Average of the two measurements") +
  ylab("Difference in the two measurements") +
  xlim(0,8000) +
  ylim(-8000,8000)

## End(Not run)

## In the above plot the spread of the differences increases with increasing
```

```
## mean of the observations. The Bland Altman limits of agreement should be
## calculated on a log scale.

logx <- log(x + 50, base = 10)
logy <- log(y + 50, base = 10)

log10.ccc <- epi.ccc(x = logx, y = logy, ci = "z-transform",
   conf.level = 0.95, rep.measure = FALSE)

## Transform the limits of agreement back to the original scale by taking
## anti-logs. If the limits of agreement for Z = log10(x) are between -a
## and +a, with a = 1.96 * s, the ratio between two measures on the original
## scale is between 10^-a and 10^a. See page 979 of Euser et al. (2008).

a <- 1.96 * log10.ccc$sblalt$delta.sd

## For a given value for the mean Xbar, it can be shown that x - y is between
## -2Xbar(10^a - 1) / (10^a + 1) and +2Xbar(10^a - 1) / (10^a + 1):

Xbar = seq(from = 0, to = 8000, by = 100)
Xbar.low <- (-2 * Xbar * (10^a - 1)) / (10^a + 1)
Xbar.upp <- (+2 * Xbar * (10^a - 1)) / (10^a + 1)
limits <- data.frame(mean = Xbar, lower = Xbar.low, upper = Xbar.upp)

## Not run:
library(ggplot2)

ggplot(crude.ccc$blalt, aes(x = mean, y = delta)) +
  geom_point() +
  geom_line(data = limits, aes(x = mean, y = lower), linetype = 2) +
  geom_line(data = limits, aes(x = mean, y = upper), linetype = 2) +
  geom_line(data = limits, aes(x = mean, y = 0), linetype = 1) +
  xlab("Average of the two measurements") +
  ylab("Difference in the two measurements") +
  xlim(0,8000) +
  ylim(-8000,8000)

## End(Not run)
```

`epi.ccsize` *Sample size, power or minimum detectable odds ratio for an unmatched or matched case-control study*

Description

Calculates the sample size, power or minimum detectable odds ratio for an unmatched or matched case-control study.

Usage

```
epi.ccsize(OR, p0, n, power, r = 1, rho = 0, design = 1, sided.test = 2,
   conf.level = 0.95, method = "unmatched", fleiss = FALSE)
```

Arguments

OR	scalar, the expected study odds ratio.
p0	scalar, the prevalence of exposure amongst the controls.
n	scalar, the total number of subjects in the study (i.e. the number of cases plus the number of controls).
power	scalar, the required study power.
r	scalar, the number in the control group divided by the number in the case group.
rho	scalar, the correlation between case and control exposures for matched pairs. This argument is ignored when method = "unmatched".
design	scalar, the design effect.
sided.test	use a one- or two-sided test? Use a two-sided test if you wish to evaluate whether or not the odds of exposure in cases is greater than or less than the controls. Use a one-sided test to evaluate whether or not the odds of exposure in cases is greater than the controls.
conf.level	scalar, the level of confidence in the computed result.
method	a character string defining the method to be used. Options are unmatched or matched.
fleiss	logical, indicating whether or not the Fleiss correction should be applied. This argument is ignored when method = "matched".

Details

This function implements the methodology described by Dupont (1988). A detailed description of sample size calculations for case-control studies (with numerous worked examples, many of them reproduced below) is provided by Woodward (2005), pp. 381 to 426.

Value

A list containing the following:

n.total	the total number of subjects required to estimate the specified odds ratio at the desired level of confidence and power (i.e. the number of cases plus the number of controls).
n.case	the total number of case subjects required to estimate the specified odds ratio at the desired level of confidence and power.
n.control	the total number of control subjects required to estimate the specified odds ratio at the desired level of confidence and power.
power	the power of the study given the number of study subjects, the specified odds ratio and the desired level of confidence.
OR	the expected detectable odds ratio given the number of study subjects, the desired power and desired level of confidence.

Note

The power of a study is its ability to demonstrate the presence of an association, given that an association actually exists.

See the documentation for epi.cohortsize which provides an example using the design facility implemented in this function.

References

Dupont WD (1988) Power calculations for matched case-control studies. Biometrics 44: 1157 - 1168.

Fleiss JL (1981). Statistical Methods for Rates and Proportions. Wiley, New York.

Kelsey JL, Thompson WD, Evans AS (1986). Methods in Observational Epidemiology. Oxford University Press, London, pp. 254 - 284.

Woodward M (2005). Epidemiology Study Design and Data Analysis. Chapman & Hall/CRC, New York, pp. 381 - 426.

Examples

```
## EXAMPLE 1 (from Woodward 2005 p. 412):
## A case-control study of the relationship between smoking and CHD is
## planned. A sample of men with newly diagnosed CHD will be compared for
## smoking status with a sample of controls. Assuming an equal number of
## cases and controls, how many study subject are required to detect an
## odds ratio of 2.0 with 0.90 power using a two-sided 0.05 test? Previous
## surveys have shown that around 0.30 of males without CHD are smokers.

epi.ccsize(OR = 2.0, p0 = 0.30, n = NA, power = 0.90, r = 1, rho = 0,
   design = 1, sided.test = 2, conf.level = 0.95, method = "unmatched",
   fleiss = FALSE)

## A total of 376 men need to be sampled: 188 cases and 188 controls.


## EXAMPLE 2 (from Woodward 2005 p. 414):
## Suppose we wish to determine the power to detect an odds ratio of 2.0
## using a two-sided 0.05 test when 188 cases and 940 controls
## are available (that is, the ratio of controls to cases is 5:1). Assume
## the prevalence of smoking in males without CHD is 0.30.

n <- 188 + 940
epi.ccsize(OR = 2.0, p0 = 0.30, n = n, power = NA, r = 5, rho = 0,
   design = 1, sided.test = 2, conf.level = 0.95, method = "unmatched",
   fleiss = TRUE)

## The power of this study, with the given sample size allocation is 0.99.

## EXAMPLE 3:
## The following statement appeared in a study proposal to identify risk
## factors for campylobacteriosis in humans:
```

```
## `We will prospectively recruit 300 culture-confirmed Campylobacter cases
## reported under the Public Health Act. We will then recruit one control per
## case from general practices of the enrolled cases, using frequency matching
## by age and sex. With exposure levels of 10% (thought to be realistic
## given past foodborne disease case control studies) this sample size
## will provide 80% power to detect an odds ratio of 2 at the 5% alpha
## level.'

## Confirm the statement that 300 case subjects will provide 80% power in
## this study.

epi.ccsize(OR = 2.0, p0 = 0.10, n = 600, power = NA, r = 1, rho = 0.01,
   design = 1, sided.test = 2, conf.level = 0.95, method = "matched",
   fleiss = TRUE)

## If the true odds ratio for Campylobacter in exposed subjects relative to
## unexposed subjects is 2.0 we will be able to reject the null hypothesis
## that this odds ratio equals 1 with probability (power) 0.826. The Type I
# error probability associated with this test of this null hypothesis is 0.05.


## EXAMPLE 4:
## We wish to conduct a case-control study to assess whether bladder cancer
## may be associated with past exposure to cigarette smoking. Cases will be
## patients with bladder cancer and controls will be patients hospitalised
## for injury. It is assumed that 20% of controls will be smokers or past
## smokers, and we wish to detect an odds ratio of 2 with power 90%.
## Three controls will be recruited for every case. How many subjects need
## to be enrolled in the study?

epi.ccsize(OR = 2.0, p0 = 0.20, n = NA, power = 0.90, r = 3, rho = 0,
   design = 1, sided.test = 2, conf.level = 0.95, method = "unmatched",
   fleiss = FALSE)

## A total of 620 subjects need to be enrolled in the study: 155 cases and
## 465 controls.

## An alternative is to conduct a matched case-control study rather than the
## unmatched design outlined above. One case will be matched to one control
## and the correlation between case and control exposures for matched pairs
## (rho) is estimated to be 0.01 (low). Using the same assumptions as those
## described above, how many study subjects will be required?

epi.ccsize(OR = 2.0, p0 = 0.20, n = NA, power = 0.90, r = 1, rho = 0.01,
   design = 1, sided.test = 2, conf.level = 0.95, method = "matched",
   fleiss = FALSE)

## A total of 456 subjects need to be enrolled in the study: 228 cases and
## 228 controls.


## EXAMPLE 5:
## Code to reproduce the isograph shown in Figure 2 in Dupont (1988):
```

```
r <- 1
p0 = seq(from = 0.05, to = 0.95, length = 50)
OR <- seq(from = 1.05, to = 6, length = 100)
dat <- expand.grid(p0 = p0, OR = OR)
dat$n.total <- NA

for(i in 1:nrow(dat)){
   dat$n.total[i] <- epi.ccsize(OR = dat$OR[i], p0 = dat$p0[i], n = NA,
   power = 0.80, r = 1, rho = 0, design = 1, sided.test = 2,
   conf.level = 0.95, method = "unmatched", fleiss = FALSE)$n.total
}

grid.n <- matrix(dat$n.total, nrow = length(p0))
breaks <- c(22:30,32,34,36,40,45,50,55,60,70,80,90,100,125,150,175,
   200,300,500,1000)

par(mar = c(5,5,0,5), bty = "n")
contour(x = p0, y = OR, z = log10(grid.n), add = FALSE, levels = log10(breaks),
   labels = breaks, xlim = c(0,1), ylim = c(1,6), las = 1, method = "flattest",
   xlab = 'Proportion of controls exposed', ylab = "Minimum OR to detect")

## Not run:
## The same plot using ggplot2:

library(ggplot2); library(directlabels)

p <- ggplot(data = dat, aes(x = p0, y = OR, z = n.total)) +
  geom_contour(aes(colour = ..level..), breaks = breaks) +
  xlab("Proportion of controls exposed") +
  ylab("Minimum OR to detect") +
  xlim(0,1) +
  ylim(1,6)

print(direct.label(p, list("far.from.others.borders", "calc.boxes",
   "enlarge.box", hjust = 1, vjust = 1, box.color = NA,
   fill = "transparent", "draw.rects")))

## End(Not run)

## EXAMPLE 6:
## From page 1164 of Dupont (1988). A matched case control study is to be
## carried out to quantify the association between exposure A and an outcome B.
## Assume the prevalence of exposure in controls is 0.60 and the
## correlation between case and control exposures for matched pairs (rho) is
## 0.20 (moderate). Assuming an equal number of cases and controls, how many
## subjects need to be enrolled into the study to detect an odds ratio of 3.0
## with 0.80 power using a two-sided 0.05 test?

epi.ccsize(OR = 3.0, p0 = 0.60, n = NA, power = 0.80, r = 1, rho = 0.2,
   design = 1, sided.test = 2, conf.level = 0.95, method = "matched",
   fleiss = FALSE)

## A total of 162 subjects need to be enrolled in the study: 81 cases and
```

```
## 81 controls. How many cases and controls are required if we select three
## controls per case?

epi.ccsize(OR = 3.0, p0 = 0.60, n = NA, power = 0.80, r = 3, rho = 0.2,
   design = 1, sided.test = 2, conf.level = 0.95, method = "matched",
   fleiss = FALSE)

## A total of 204 subjects need to be enrolled in the study: 51 cases and
## 153 controls.
```

`epi.cluster1size` *Sample size under under one-stage cluster sampling*

Description

Returns the required number of clusters to be sampled using a one-stage cluster sampling strategy.

Usage

```
epi.cluster1size(n, mean, var, epsilon.r, method = "mean",
   conf.level = 0.95)
```

Arguments

`n`	integer, representing the total number of clusters in the population.
`mean`	number, representing the population mean of the variable of interest.
`var`	number, representing the population variance of the variable of interest.
`epsilon.r`	the maximum relative difference between our estimate and the unknown population value.
`method`	a character string indicating the method to be used. Options are `total`, `mean` or `mean.per.unit`.
`conf.level`	scalar, defining the level of confidence in the computed result.

Value

Returns an integer defining the required number of clusters to be sampled.

References

Levy PS, Lemeshow S (1999). Sampling of Populations Methods and Applications. Wiley Series in Probability and Statistics, London, pp. 258.

Examples

```
## A survey to estimate the total number of residents over 65 years of
## age that require the services of a nurse is to be carried out. There are
## five housing complexes in the study area and we expect that there might
## be a total of around 34 residents meeting this criteria (variance 6.8).
## We would like the estimated sample size to provide us with an estimate
## that is within 10% of the true value. How many housing complexes (clusters)
## should be sampled?

epi.cluster1size(n = 5, mean = 34, var = 6.8, epsilon.r = 0.10, method =
   "total", conf.level = 0.999)

## We would need to sample 3 housing complexes to meet the specifications
## for this study.
```

---

epi.cluster2size *Sample size under under two-stage cluster sampling*

Description

Returns the required number of clusters to be sampled using a two-stage cluster sampling strategy.

Usage

```
epi.cluster2size(nbar, R, n, mean, sigma2.x, sigma2.y, sigma2.xy,
   epsilon.r, method = "mean", conf.level = 0.95)
```

Arguments

nbar	integer, representing the total number of listing units to be selected from each cluster.
R	scalar, representing an estimate of the unknown population prevalence to be estimated. Only used when `method = "proportion"`.
n	vector of length two, specifying the total number of clusters in the population and the total number of listing units within each cluster, respectively.
mean	vector of length two, specifying the mean of the variable of interest at the cluster level and listing unit level, respectively.
sigma2.x	vector of length two, specifying the variance of the [denomoniator] variable of interest at the cluster level and listing unit level, respectively.
sigma2.y	vector of length two, specifying the variance of the numerator variable of interest at the cluster level and listing unit level, respectively. See details. Only used when `method = "proportion"`.
sigma2.xy	vector of length two, specifying the the covariance at the cluster level and listing unit level, respectively. Only used when `method = "proportion"`.

epsilon.r	the maximum relative difference between the estimate and the unknown population value.
method	a character string indicating the method to be used. Options are total, mean or proportion.
conf.level	scalar, defining the level of confidence in the computed result.

Details

In simple two-stage cluster sampling the number of listing units to be selected from each cluster is determined on the basis of cost and on the basis of the relative sizes of the first- and second-stage variance components. Once the number of listing units is fixed we might then wish to determine the total number of clusters to be sampled to be confident of obtaining estimates that reflect the true population value.

Value

Returns an integer defining the required number of clusters to be sampled.

References

Levy PS, Lemeshow S (1999). Sampling of Populations Methods and Applications. Wiley Series in Probability and Statistics, London, pp. 292.

Examples

```
## EXAMPLE 1 (from Levy and Lemeshow p 292):
## We intend to conduct a survey of nurse practitioners to estimate the
## average number of patients seen by each nurse. There are five health
## centres in the study area, each with three nurses. We intend to sample
## two nurses from each health centre. We would like to be 95% confident
## that our estimate is within 30% of the true population value. We expect
## that the mean number of patients seen at the health centre level
## is 84 (var 567) and the mean number of patients seen at the nurse
## level is 28 (var 160). How many health centres should be sampled?

tn <- c(5, 3); tmean <- c(84, 28); tsigma2.x <- c(567, 160)

epi.cluster2size(nbar = 2, n = tn, mean = tmean, sigma2.x = tsigma2.x,
   sigma2.y = NA, sigma2.xy = NA, epsilon.r = 0.3, method = "mean",
   conf.level = 0.95)

## Three health centres need to be sampled to meet the survey
## specifications.


## EXAMPLE 2 (from Levy and Lemeshow p 294):
## Same scenario as above, but this time we want to estimate the proportion
## of patients referred to a general practitioner from each clinic. As before,
## we want to be 95% confident that our estimate of the proportion of referred
## patients is within 30% of the true population value. We expect that
## approximately 36% of patients are referred.
```

```
## On page 295 Levy and Lemeshow state that the parameters sigma2.x, sigma2.y
## and sigma2.xy are rarely known in advance and must be either estimated
## or guessed from experience or intuition. In this example (for
## demonstration) we use the actual patient data to calculate sigma2.x,
## sigma2.y and sigma2.xy.

## Nurse-level data. The following code reproduces Table 10.4 of Levy and
## Lemeshow (page 293).
clinic <- rep(1:5, each = 3)
nurse <- 1:15
Xij <- c(58,44,18,42,53,10,13,18,37,16,32,10,25,23,23)
Yij <- c(5,6,6,3,19,2,12,6,30,5,14,4,17,9,14)
ssudat <- data.frame(clinic, nurse, Xij, Yij)

Xbar <- by(data = ssudat$Xij, INDICES = ssudat$clinic, FUN = mean)
ssudat$Xbar <- rep(Xbar, each = 3)
Ybar <- by(data = ssudat$Yij, INDICES = ssudat$clinic, FUN = mean)
ssudat$Ybar <- rep(Ybar, each = 3)

ssudat$Xij.Xbar <- (ssudat$Xij - ssudat$Xbar)^2
ssudat$Yij.Ybar <- (ssudat$Yij - ssudat$Ybar)^2
ssudat$XY <- (ssudat$Xij - ssudat$Xbar) * (ssudat$Yij - ssudat$Ybar)

## Collapse the nurse-level data (created above) to the clinic level.
## The following code reproduces Table 10.3 of Levy and Lemeshow (page 292).
clinic <- as.vector(by(ssudat$clinic, INDICES = ssudat$clinic, FUN = min))
Xi <- as.vector(by(ssudat$Xij, INDICES = ssudat$clinic, FUN = sum))
Yi <- as.vector(by(ssudat$Yij, INDICES = ssudat$clinic, FUN = sum))
psudat <- data.frame(clinic, Xi, Yi)

psudat$Xi.Xbar <- (psudat$Xi - mean(psudat$Xi))^2
psudat$Yi.Ybar <- (psudat$Yi - mean(psudat$Yi))^2
psudat$XY <- (psudat$Xi - mean(psudat$Xi)) * (psudat$Yi - mean(psudat$Yi))

## Number of primary and secondary sampling units:
npsu <- nrow(psudat)
nssu <- mean(by(ssudat$nurse, INDICES = ssudat$clinic, FUN = length))
tn <- c(npsu, nssu)

## Mean of X at primary sampling unit and secondary sampling unit level:
tmean <- c(mean(psudat$Xi), mean(ssudat$Xij))

## Variance of number of patients seen:
tsigma2.x <- c(mean(psudat$Xi.Xbar), mean(ssudat$Xij.Xbar))

## Variance of number of patients referred:
tsigma2.y <- c(mean(psudat$Yi.Ybar), mean(ssudat$Yij.Ybar))
tsigma2.xy <- c(mean(psudat$XY), mean(ssudat$XY))

epi.cluster2size(nbar = 2, R = 0.36, n = tn, mean = tmean,
   sigma2.x = tsigma2.x, sigma2.y = tsigma2.y, sigma2.xy = tsigma2.xy,
   epsilon.r = 0.3, method = "proportion", conf.level = 0.95)
```

```
## Two health centres need to be sampled to meet the survey
## specifications.


## EXAMPLE 3:
## We want to determine the prevalence of brucellosis in dairy cattle in a
## country comprised of 20 provinces. The number of dairy herds per province
## ranges from 50 to 1200. Herd size ranges from 25 to 900. We suspect that
## the prevalence of brucellosis-positive herds across the entire country
## is around 10%. We suspect that there are a small number of provinces
## with a relatively high individual cow-level prevalence of disease
## (thought to be between 40% and 80%). How many herds should be sampled
## from each province if we want our estimate of prevalence to be within
## 30% of the true population value?

epi.simplesize(N = 1200, Vsq = NA, Py = 0.10, epsilon.r = 0.30,
   method = "proportion", conf.level = 0.95)

## A total of 234 herds should be sampled from each province.

## Next we work out the number of provinces that need to be sampled.
## Again, we would like to be 95% confident that our estimate is within
## 30% of the true population value. Simulate some data to derive appropriate
## estimates of sigma2.x, sigma2.y and sigma2.xy.

## Number of herds per province:
npsu <- 20
nherds.p <- as.integer(runif(n = npsu, min = 50, max = 1200))

## Mean herd size per province:
hsize.p <- as.integer(runif(n = npsu, min = 25, max = 900))

## Simulate estimates of the cow-level prevalence of brucellosis in each
## province. Here we generate an equal mix of `low' and `high' brucellosis
## prevalence provinces:
prev.p <- c(runif(n = 15, min = 0, max = 0.05),
   runif(n = 5, min = 0.40, max = 0.80))

## Generate some data:
prov <- c(); herd <- c();
Xij <- c(); Yij <- c();
Xbar <- c(); Ybar <- c();
Xij.Xbar <- c(); Yij.Ybar <- c()

for(i in 1:npsu){
   ## Province identifiers:
   tprov <- rep(i, times = nherds.p[i])
   prov <- c(prov, tprov)

   ## Herd identifiers:
   therd <- 1:nherds.p[i]
   herd <- c(herd, therd)
```

```
   ## Number of cows in each of the herds in this province:
   tXij <- as.integer(rlnorm(n = nherds.p[i], meanlog = log(hsize.p[i]),
      sdlog = 0.5))
   tXbar <- mean(tXij)
   tXij.Xbar <- (tXij - tXbar)^2
   Xij <- c(Xij, tXij)
   Xbar <- c(Xbar, rep(tXbar, times = nherds.p[i]))
   Xij.Xbar <- c(Xij.Xbar, tXij.Xbar)

   ## Number of brucellosis-positive cows in each herd:
   tYij <- c()
   for(j in 1:nherds.p[i]){
      ttYij <- rbinom(n = 1, size = tXij[j], prob = prev.p[i])
      tYij <- c(tYij, ttYij)
      }
    tYbar <- mean(tYij)
    tYij.Ybar <- (tYij - tYbar)^2
    Yij <- c(Yij, tYij)
    Ybar <- c(Ybar, rep(tYbar, times = nherds.p[i]))
    Yij.Ybar <- c(Yij.Ybar, tYij.Ybar)
}

ssudat <- data.frame(prov, herd, Xij, Yij, Xbar, Ybar, Xij.Xbar, Yij.Ybar)
ssudat$XY <- (ssudat$Xij - ssudat$Xbar) * (ssudat$Yij - ssudat$Ybar)

## Collapse the herd-level data (created above) to the province level:
prov <- as.vector(by(ssudat$prov, INDICES = ssudat$prov, FUN = min))
Xi <- as.vector(by(ssudat$Xij, INDICES = ssudat$prov, FUN = sum))
Yi <- as.vector(by(ssudat$Yij, INDICES = ssudat$prov, FUN = sum))
psudat <- data.frame(prov, Xi, Yi)

psudat$Xi.Xbar <- (psudat$Xi - mean(psudat$Xi))^2
psudat$Yi.Ybar <- (psudat$Yi - mean(psudat$Yi))^2
psudat$XY <- (psudat$Xi - mean(psudat$Xi)) * (psudat$Yi - mean(psudat$Yi))

## Number of primary and secondary sampling units:
npsu <- nrow(psudat)
nssu <- round(mean(by(ssudat$herd, INDICES = ssudat$prov, FUN = length)),
   digits = 0)
tn <- c(npsu, nssu)

## Mean of X at primary sampling unit and secondary sampling unit level:
tmean <- c(mean(psudat$Xi), mean(ssudat$Xij))

## Variance of herd size:
tsigma2.x <- c(mean(psudat$Xi.Xbar), mean(ssudat$Xij.Xbar))

## Variance of number of brucellosis-positive cows:
tsigma2.y <- c(mean(psudat$Yi.Ybar), mean(ssudat$Yij.Ybar))
tsigma2.xy <- c(mean(psudat$XY), mean(ssudat$XY))

## Finally, calculate the number of provinces to be sampled:
```

```
tR <- sum(psudat$Yi) / sum(psudat$Xi)

epi.cluster2size(nbar = 234, R = tR, n = tn, mean = tmean,
   sigma2.x = tsigma2.x, sigma2.y = tsigma2.y, sigma2.xy = tsigma2.xy,
   epsilon.r = 0.3, method = "proportion", conf.level = 0.95)

## Four provinces (sampling 234 herds from each) are required to be 95%
## confident that our estimate of the individual animal prevalence of
## brucellosis is within 30% of the true population value.
```

`epi.clustersize` *Sample size for cluster-sample surveys*

Description

Estimates the number of clusters to be sampled using a cluster-sample design.

Usage

```
epi.clustersize(p, b, rho, epsilon.r, conf.level = 0.95)
```

Arguments

`p`	the estimated prevalence of the outcome in the population.
`b`	the number of units sampled per cluster.
`rho`	the intra-cluster correlation, a measure of the variation between clusters compared with the variation within clusters.
`epsilon.r`	scalar, the acceptable relative error.
`conf.level`	scalar, defining the level of confidence in the computed result.

Value

A list containing the following:

`clusters`	the estimated number of clusters to be sampled.
`units`	the total number of units to be sampled.
`design`	the design effect.

Note

The intra-cluster correlation (`rho`) will be higher for those situations where the between-cluster variation is greater than within-cluster variation. The design effect depends on `rho` and `b` (the number of units sampled per cluster). Note that `b` is the number of units sampled per cluster, not the total number of units per cluster. `rho = (D - 1) / (b - 1)`.

Design effects of 2, 4, and 7 can be used to estimate `rho` when intra-cluster correlation is low, medium, and high (respectively). A design effect of 7.5 should be used when the intra-cluster correlation is unknown.

References

Bennett S, Woods T, Liyanage WM, Smith DL (1991). A simplified general method for cluster-sample surveys of health in developing countries. World Health Statistics Quarterly 44: 98 - 106.

Otte J, Gumm I (1997). Intra-cluster correlation coefficients of 20 infections calculated from the results of cluster-sample surveys. Preventive Veterinary Medicine 31: 147 - 150.

Examples

```
## EXAMPLE 1:
## The expected prevalence of disease in a population of cattle is 0.10.
## We wish to conduct a survey, sampling 50 animals per farm. No data
## are available to provide an estimate of rho, though we suspect
## the intra-cluster correlation for this disease to be moderate.
## We wish to be 95% certain of being within 10% of the true population
## prevalence of disease. How many herds should be sampled?

p <- 0.10; b <- 50; D <- 4
rho <- (D - 1) / (b - 1)
epi.clustersize(p = 0.10, b = 50, rho = rho, epsilon.r = 0.10,
   conf.level = 0.95)

## We need to sample 278 herds (13900 samples in total).

## EXAMPLE 2 (from Bennett et al. 1991):
## A cross-sectional study is to be carried out to determine the prevalence
## of a given disease in a population using a two-stage cluster design. We
## estimate prevalence to be 0.20 and we expect rho to be in the order of 0.02.
## We want to take sufficient samples to be 95% certain that our estimate of
## prevalence is within 5% of the true population value (that is, a relative
## error of 0.05 / 0.20 = 0.25). Assuming 20 responses from each cluster,
## how many clusters do we need to be sample?

epi.clustersize(p = 0.20, b = 20, rho = 0.02, epsilon.r = 0.25,
   conf.level = 0.95)

## We need to sample 18 clusters (360 samples in total).
```

---

epi.cohortsize *Sample size, power or minimum detectable risk ratio for a cohort study*

Description

Calculates the sample size, power or minimum detectable risk ratio for a cohort study.

Usage

```
epi.cohortsize(exposed, unexposed, n, power, r = 1, design = 1, sided.test = 2,
   conf.level = 0.95)
```

Arguments

exposed	the expected incidence risk (cumulative incidence) for exposed subjects (see below).
unexposed	the expected incidence risk (cumulative incidence) for unexposed subjects (see below).
n	scalar, defining the total number of subjects in the study (i.e. the number in the exposed and unexposed groups).
power	scalar, the required study power.
r	scalar, the number in the treatment group divided by the number in the control group. This argument is ignored when method = "proportions".
design	scalar, the estimated design effect.
sided.test	use a one- or two-sided test? Use a two-sided test if you wish to evaluate whether or not the treatment group is better or worse than the control group. Use a one-sided test to evaluate whether or not the treatment group is better than the control group.
conf.level	scalar, defining the level of confidence in the computed result.

Details

The methodology in this function follows the approach described in Chapter 8 of Woodward (2005), pp. 381 - 426.

Value

A list containing the following:

n.total	the total number of subjects required for the specified level of confidence and power, respecting the requirement for r times as many individuals in the treatment group compared with the control group.
n.treat	the total number of subjects in the treatment group for the specified level of confidence and power, respecting the requirement for r times as many individuals in the treatment group compared with the control group.
n.control	the total number of subjects in the control group for the specified level of confidence and power, respecting the requirement for r times as many individuals in the treatment group compared with the control group.
power	the power of the study given the number of study subjects, the expected effect size and level of confidence.
lambda	the outcome proportion in the exposed group divided by the outcome proportion in the unexposed group (a risk ratio).

Note

The power of a study is its ability to demonstrate the presence of an association, given that an association actually exists.

Values need to be entered for unexposed, n, and power to return a value for lambda. In this situation, the lower value of lambda represents the maximum detectable risk ratio that is less than 1; the upper value of lambda represents the minimum detectable risk ratio greater than 1.

References

Kelsey JL, Thompson WD, Evans AS (1986). Methods in Observational Epidemiology. Oxford University Press, London, pp. 254 - 284.

Woodward M (2005). Epidemiology Study Design and Data Analysis. Chapman & Hall/CRC, New York, pp. 381 - 426.

Examples

```
## EXAMPLE 1 (from Woodward 2005 p. 406):
## A cohort study of smoking and coronary heart disease (CHD) in middle aged men
## is planned. A sample of men will be selected at random from the population
## and those that agree to participate will be asked to complete a
## questionnaire. The follow-up period will be 5 years. The investigators would
## like to be 0.90 sure of being able to detect when the risk ratio of CHD
## is 1.4 for smokers, using a 0.05 significance test. Previous evidence
## suggests that the incidence risk of death rate in non-smokers is 413 per
## 100,000 per year. Assuming equal numbers of smokers and non-smokers are
## sampled, how many men should be sampled overall?

e1 = 1.4 * (5 * 413)/100000; e0 = (5 * 413)/100000
epi.cohortsize(exposed = e1, unexposed = e0, n = NA, power = 0.90,
   r = 1, design = 1, sided.test = 1, conf.level = 0.95)

## A total of 12,130 men need to be sampled (6065 smokers and 6065 non-smokers).


## EXAMPLE 2 (from Woodward 2005 p. 406):
## Say, for example, we are only able to enrol 5000 subjects into the study
## described above. What is the minimum and maximum detectable risk ratio?

e0 = (5 * 413)/100000
epi.cohortsize(exposed = NA, unexposed = e0, n = 5000, power = 0.90,
   r = 1, design = 1, sided.test = 1, conf.level = 0.95)

## The minimum detectable risk ratio >1 is 1.65. The maximum detectable
## risk ratio <1 is 0.50.


## EXAMPLE 3:
## A study is to be carried out to assess the effect of a new treatment for
## anoestrus in dairy cattle. What is the required sample size if we expect
## the proportion of cows responding in the treatment (exposed) group to be
## 0.30 and the proportion of cows responding in the control (unexposed) group
## to be 0.15? The required power for this study is 0.80 using a two-sided
## 0.05 test.

epi.cohortsize(exposed = 0.30, unexposed = 0.15, n = NA, power = 0.80,
   r = 1, design = 1, sided.test = 2, conf.level = 0.95)

## A total of 242 cows are required: 121 in the treatment (exposed) group and
## 121 in the control (unexposed) group.
```

```
## Assume now that this study is going to be carried out using animals from a
## number of herds. What is the required sample size when you account for the
## observation that response to treatment is likely to cluster within herds.

## For the exercise, assume that the intra-cluster correlation coefficient
## (the rate of homogeneity, rho) for this treatment is 0.05 and the
## average number of cows sampled per herd will be 30.

## Calculate the design effect, given rho = (design - 1) / (nbar - 1),
## where nbar equals the average number of individuals per cluster:

design <- 0.05 * (30 - 1) + 1
epi.cohortsize(exposed = 0.30, unexposed = 0.15, n = NA, power = 0.80,
   r = 1, design = design, sided.test = 2, conf.level = 0.95)

## A total of 592 cows are required for this study: 296 in the treatment group
## and 296 in the control group.
```

`epi.conf` *Confidence intervals for means, proportions, incidence, and standardised mortality ratios*

Description

Computes confidence intervals for means, proportions, incidence, and standardised mortality ratios.

Usage

```
epi.conf(dat, ctype = "mean.single", method, N, design = 1,
   conf.level = 0.95)
```

Arguments

`dat`	the data, either a vector or a matrix depending on the method chosen.
`ctype`	a character string indicating the type of confidence interval to calculate. Options are `mean.single`, `mean.unpaired`, `mean.paired`, `prop.single`, `prop.unpaired`, `prop.paired`, `prevalence`, `inc.risk`, `inc.rate`, `odds`, `ratio` and `smr`.
`method`	a character string indicating the method to use. Where `ctype = "inc.risk"` or `ctype = "prevalence"` options are `exact`, `wilson` and `fleiss`. Where `ctype = "inc.rate"` options are `exact` and `byar`.
`N`	scalar, representing the population size.
`design`	scalar, representing the design effect.
`conf.level`	magnitude of the returned confidence interval. Must be a single number between 0 and 1.

Details

Method mean.single requires a vector as input. Method `mean.unpaired` requires a two-column data frame; the first column defining the groups must be a factor. Method `mean.paired` requires a two-column data frame; one column for each group. Method `prop.single` requires a two-column matrix; the first column specifies the number of positives, the second column specifies the number of negatives. Methods `prop.unpaired` and `prop.paired` require a four-column matrix; columns 1 and 2 specify the number of positives and negatives for the first group, columns 3 and 4 specify the number of positives and negatives for the second group. Method `prevalence` and `inc.risk` require a two-column matrix; the first column specifies the number of positives, the second column specifies the total number tested. Method `inc.rate` requires a two-column matrix; the first column specifies the number of positives, the second column specifies individual time at risk. Method `odds` requires a two-column matrix; the first column specifies the number of positives, the second column specifies the number of negatives. Method `ratio` requires a two-column matrix; the first column specifies the numerator, the second column specifies the denominator. Method `smr` requires a two-colum matrix; the first column specifies the total number of positives, the second column specifies the total number tested.

The methodology implemented here follows Altman, Machin, Bryant, and Gardner (2000). Where method is `inc.risk`, `prevalence` or `inc.rate` if the numerator equals zero the lower bound of the confidence interval estimate is set to zero. Where method is `smr` the method of Dobson et al. (1991) is used. A summary of the methods used for each of the confidence interval calculations in this function is as follows:

ctype-method	Reference
mean.single	Altman et al. (2000)
mean.unpaired	Altman et al. (2000)
mean.paired	Altman et al. (2000)
prop.single	Altman et al. (2000)
prop.unpaired	Altman et al. (2000)
prop.paired	Altman et al. (2000)
inc.risk, exact	Collett (1999)
inc.risk, wilson	Rothman (2002)
inc.risk, fleiss	Fleiss (1981)
prevalence, exact	Collett (1999)
prevalence, wilson	Rothman (2002)
prevalence, fleiss	Fleiss (1981)
inc.rate, exact	Collett (1999)
inc.rate, byar	Rothman (2002)
odds	Ederer and Mantel (1974)
ratio	Ederer and Mantel (1974)
smr	Dobson et al. (1991)

The design effect is used to adjust the confidence interval around a prevalence or incidence risk estimate in the presence of clustering. The design effect is a measure of the variability between clusters and is calculated as the ratio of the variance calculated assuming a complex sample design

divided by the variance calculated assuming simple random sampling. Adjustment for the effect of clustering can only be done on those prevalence and incidence risk methods that return a standard error (i.e. `method = "wilson"` or `method = "fleiss"`).

References

Altman DG, Machin D, Bryant TN, and Gardner MJ (2000). Statistics with Confidence, second edition. British Medical Journal, London, pp. 28 - 29 and pp. 45 - 56.

Collett D (1999). Modelling Binary Data. Chapman & Hall/CRC, Boca Raton Florida, pp. 24.

Dobson AJ, Kuulasmaa K, Eberle E, and Scherer J (1991). Confidence intervals for weighted sums of Poisson parameters. Statistics in Medicine 10: 457 - 462.

Ederer F, and Mantel N (1974). Confidence limits on the ratio of two Poisson variables. American Journal of Epidemiology 100: 165 - 167

Fleiss JL (1981). Statistical Methods for Rates and Proportions. 2nd edition. John Wiley & Sons, New York.

Killip S, Mahfoud Z, Pearce K (2004). What is an intracluster correlation coefficient? Crucial concepts for primary care researchers. Annals of Family Medicine 2: 204 - 208.

Otte J, Gumm I (1997). Intra-cluster correlation coefficients of 20 infections calculated from the results of cluster-sample surveys. Preventive Veterinary Medicine 31: 147 - 150.

Rothman KJ (2002). Epidemiology An Introduction. Oxford University Press, London, pp. 130 - 143.

Examples

```
## EXAMPLE 1:
dat <- rnorm(n = 100, mean = 0, sd = 1)
epi.conf(dat, ctype = "mean.single")

## EXAMPLE 2:
group <- c(rep("A", times = 5), rep("B", times = 5))
val = round(c(rnorm(n = 5, mean = 10, sd = 5),
   rnorm(n = 5, mean = 7, sd = 5)), digits = 0)
dat <- data.frame(group = group, val = val)
epi.conf(dat, ctype = "mean.unpaired")

## EXAMPLE 3:
## Two paired samples (Altman et al. 2000, page 31):
## Systolic blood pressure levels were measured in 16 middle-aged men
## before and after a standard exercise test. The mean rise in systolic
## blood pressure was 6.6 mmHg. The standard deviation of the difference
## was 6.0 mm Hg. The standard error of the mean difference was 1.49 mm Hg.

before <- c(148,142,136,134,138,140,132,144,128,170,162,150,138,154,126,116)
after <- c(152,152,134,148,144,136,144,150,146,174,162,162,146,156,132,126)
dat <- data.frame(before, after)
dat <- data.frame(cbind(before, after))
epi.conf(dat, ctype = "mean.paired", conf.level = 0.95)

## The 95% confidence interval for the population value of the mean
```

```
## systolic blood pressure increase after standard exercise was 3.4 to 9.8
## mm Hg.

## EXAMPLE 4:
## Single sample (Altman et al. 2000, page 47):
## Out of 263 giving their views on the use of personal computers in
## general practice, 81 thought that the privacy of their medical file
## had been reduced.

pos <- 81
neg <- (263 - 81)
dat <- as.matrix(cbind(pos, neg))
round(epi.conf(dat, ctype = "prop.single"), digits = 3)

## The 95% confidence interval for the population value of the proportion
## of patients thinking their privacy was reduced was from 0.255 to 0.366.

## EXAMPLE 5:
## Two samples, unpaired (Altman et al. 2000, page 49):
## Goodfield et al. report adverse effects in 85 patients receiving either
## terbinafine or placebo treatment for dermatophyte onchomychois.
## Out of 56 patients receiving terbinafine, 5 patients experienced
## adverse effects. Out of 29 patients receiving a placebo, none experienced
## adverse effects.

grp1 <- matrix(cbind(5, 51), ncol = 2)
grp2 <- matrix(cbind(0, 29), ncol = 2)
dat <- as.matrix(cbind(grp1, grp2))
round(epi.conf(dat, ctype = "prop.unpaired"), digits = 3)

## The 95% confidence interval for the difference between the two groups is
## from -0.038 to +0.193.

## EXAMPLE 6:
## Two samples, paired (Altman et al. 2000, page 53):
## In a reliability exercise, 41 patients were randomly selected from those
## who had undergone a thalium-201 stress test. The 41 sets of images were
## classified as normal or not by the core thalium laboratory and,
## independently, by clinical investigators from different centres.
## Of the 19 samples identified as ischaemic by clinical investigators
## 5 were identified as ischaemic by the laboratory. Of the 22 samples
## identified as normal by clinical investigators 0 were identified as
## ischaemic by the laboratory.

## Clinic       | Laboratory    |             |
##              | Ischaemic     | Normal      | Total
## ------------------------------------------------------------
##  Ischaemic   | 14            | 5           | 19
##  Normal      | 0             | 22          | 22
## ------------------------------------------------------------
##  Total       | 14            | 27          | 41
## ------------------------------------------------------------
```

```
dat <- as.matrix(cbind(14, 5, 0, 22))
round(epi.conf(dat, ctype = "prop.paired", conf.level = 0.95), digits = 3)

## The 95% confidence interval for the population difference in
## proportions is 0.011 to 0.226 or approximately +1% to +23%.

## EXAMPLE 7:
## A herd of 1000 cattle were tested for brucellosis. Four samples out of 200
## test returned a positive result. Assuming 100% test sensitivity and
## specificity, what is the estimated prevalence of brucellosis in this
## group of animals?

pos <- 4; pop <- 200
dat <- as.matrix(cbind(pos, pop))
epi.conf(dat, ctype = "prevalence", method = "exact", N = 1000,
   design = 1, conf.level = 0.95) * 100

## The estimated prevalence of brucellosis in this herd is 2 cases
## per 100 cattle (95% CI 0.54 -- 5.0 cases per 100 cattle).

## EXAMPLE 8:
## The observed disease counts and population size in four areas are provided
## below. What are the the standardised morbidity ratios of disease for each
## area and their 95% confidence intervals?

obs <- c(5, 10, 12, 18); pop <- c(234, 189, 432, 812)
dat <- as.matrix(cbind(obs, pop))
round(epi.conf(dat, ctype = "smr"), digits = 2)

## EXAMPLE 9:
## A survey has been conducted to determine the proportion of broilers
## protected from a given disease following vaccination. We assume that
## the intra-cluster correlation coefficient for protection (also known as the
## rate of homogeneity, rho) is 0.4 and the average number of birds per
## flock is 30. A total of 5898 birds from a total of 10363 were identified
## as protected. What proportion of birds are protected and what is the 95%
## confidence interval for this estimate?

## Calculate the design effect, given rho = (design - 1) / (nbar - 1), where
## nbar equals the average number of individuals sampled per cluster:

D <- 0.4 * (30 - 1) + 1

## The design effect is 12.6. Now calculate the proportion protected:

dat <- as.matrix(cbind(5898, 10363))
epi.conf(dat, ctype = "prevalence", method = "fleiss", N = 1000000,
   design = D, conf.level = 0.95)

## The estimated proportion of the population protected is 0.57 (95% CI
## 0.53 -- 0.60). If we had mistakenly assumed that data were a simple random
## sample the confidence interval would have been 0.56 -- 0.58.
```

epi.convgrid — *Convert British National Grid georeferences to easting and northing coordinates*

Description

Convert British National Grid georeferences to easting and northing coordinates.

Usage

```
epi.convgrid(os.refs)
```

Arguments

os.refs	a vector of character strings listing the British National Grid georeferences to be converted.

Note

If an invalid georeference is encountered in the vector os.ref the method returns a NA.

Examples

```
os.refs <- c("SJ505585","SJ488573","SJ652636")
epi.convgrid(os.refs)
```

epi.cp — *Extract unique covariate patterns from a data set*

Description

Extract the set of unique patterns from a set of covariates.

Usage

```
epi.cp(dat)
```

Arguments

dat	an *i* row by *j* column data frame where the *i* rows represent individual observations and the *m* columns represent a set of *m* covariates. The function permits one or more covariates for each observation.

Details

This function extracts the k unique covariate patterns in a data set comprised of i observations, labelling them from 1 to k. The frequency of occurrence of each covariate pattern is listed. A vector of length i is also returned, listing the 1:k covariate pattern identifier for each observation.

Value

A list containing the following:

`cov.pattern`	a data frame with columns: `id` the unique covariate pattern identifier (labelled 1 to k), `n` the number of occasions each of the listed covariate pattern appears in the data, and the unique covariate combinations.
`id`	a vector of length i listing the 1:k covariate pattern identifier for each observation.

Author(s)

Thanks to Johann Popp and Mathew Jay for providing code and suggestions to enhance the utility of this function.

References

Dohoo I, Martin W, Stryhn H (2003). Veterinary Epidemiologic Research. AVC Inc, Charlottetown, Prince Edward Island, Canada.

Examples

```
## Generate a set of covariates:
set.seed(seed = 1234)
obs <- round(runif(n = 100, min = 0, max = 1), digits = 0)
v1 <- round(runif(n = 100, min = 0, max = 4), digits = 0)
v2 <- round(runif(n = 100, min = 0, max = 4), digits = 0)
dat <- data.frame(obs, v1, v2)

dat.glm <- glm(obs ~ v1 + v2, family = binomial, data = dat)
dat.mf <- model.frame(dat.glm)

## Covariate pattern:
epi.cp(dat.mf[-1])

## There are 25 covariate patterns in this data set. Subject 100 has
## covariate pattern 21.
```

epi.cpresids *Covariate pattern residuals from a logistic regression model*

Description

Returns covariate pattern residuals and delta betas from a logistic regression model.

Usage

```
epi.cpresids(obs, fit, covpattern)
```

Arguments

obs	a vector of observed values (i.e. counts of 'successes') for each covariate pattern).
fit	a vector defining the predicted (i.e. fitted) probability of success for each covariate pattern.
covpattern	a epi.cp object.

Value

A data frame with 13 elements: cpid the covariate pattern identifier, n the number of subjects in this covariate pattern, obs the observed number of successes, pred the predicted number of successes, raw the raw residuals, sraw the standardised raw residuals, pearson the Pearson residuals, spearson the standardised Pearson residuals, deviance the deviance residuals, leverage leverage, deltabeta the delta-betas, sdeltabeta the standardised delta-betas, and deltachi delta chi statistics.

References

Hosmer DW, Lemeshow S (1989). Applied Logistic Regression. John Wiley & Sons, New York, USA, pp. 137 - 138.

See Also

epi.cp

Examples

```
infert.glm <- glm(case ~ spontaneous + induced, data = infert,
   family = binomial())

infert.mf <- model.frame(infert.glm)
infert.cp <- epi.cp(infert.mf[-1])

infert.obs <- as.vector(by(infert$case, as.factor(infert.cp$id),
   FUN = sum))
infert.fit <- as.vector(by(fitted(infert.glm), as.factor(infert.cp$id),
```

```
   FUN = min))
infert.res <- epi.cpresids(obs = infert.obs, fit = infert.fit,
   covpattern = infert.cp)
```

`epi.descriptives` *Descriptive statistics*

Description

Computes descriptive statistics from a vector of numbers.

Usage

```
epi.descriptives(dat, conf.level = 0.95)
```

Arguments

`dat`	vector for which descriptive statistics will be calculated.
`conf.level`	magnitude of the returned confidence intervals. Must be a single number between 0 and 1.

Value

A list containing the following:

`arithmetic`	`n` number of observations, `mean` arithmetic mean, `sd` arithmetic standard deviation, `q25` 25th quantile, `q50` 50th quantile, `q75` 75th quantile, `lower` lower bound of the confidence interval, `upper` upper bound of the confidence interval, `min` minimum value, `max` maximum value, and `na` number of missing values.
`geometric`	`n` number of observations, `mean` geometric mean, `sd` geometric standard deviation, `q25` 25th quantile, `q50` 50th quantile, `q75` 75th quantile, `lower` lower bound of the confidence interval, `upper` upper bound of the confidence interval, `min` minimum value, `max` maximum value, and `na` number of missing values.
`symmetry`	`skewness` and `kurtosis`.

Examples

```
id <- 1:1000
tmp <- rnorm(1000, mean = 0, sd = 1)
id <- sample(id, size = 20)
tmp[id] <- NA

epi.descriptives(tmp, conf.level = 0.95)
```

`epi.detectsize` *Sample size to detect disease*

Description

Estimates the required sample size to detect disease. The method adjusts sample size estimates on the basis of test sensitivity and specificity and can account for series and parallel test interpretation.

Usage

```
epi.detectsize(N, prev, se, sp, interpretation = "series",
   covar = c(0,0), conf.level = 0.95, finite.correction = TRUE)
```

Arguments

`N`	a vector of length one or two defining the size of the population. The first element of the vector defines the number of clusters, the second element defining the mean number of sampling units per cluster.
`prev`	a vector of length one or two defining the prevalence of disease in the population. The first element of the vector defines the between-cluster prevalence, the second element defines the within-cluster prevalence.
`se`	a vector of length one or two defining the sensitivity of the test(s) used.
`sp`	a vector of length one or two defining the specificity of the test(s) used.
`interpretation`	a character string indicating how test results should be interpreted. Options are `series` or `parallel`.
`covar`	a vector of length two defining the covariance between test results for disease positive and disease negative groups. The first element of the vector is the covariance between test results for disease positive subjects. The second element of the vector is the covariance between test results for disease negative subjects. Use `covar = c(0,0)` (the default) if these values are not known.
`conf.level`	scalar, defining the level of confidence in the computed result.
`finite.correction`	logical, should a finite correction factor be applied?

Value

A list containing the following:

`performance`	The sensitivity and specificity of the testing strategy.
`sample.size`	The number of clusters, units, and total number of units to be sampled.

Note

The finite correction factor reduces the variance of the sample as the sample size approaches the population size. As a rule of thumb, set `finite.correction = TRUE` when the sample size is greater than 5% of the population size.

Define `se1` and `se2` as the sensitivity for the first and second test, `sp1` and `sp2` as the specificity for the first and second test, `p111` as the proportion of disease-positive subjects with a positive test result to both tests and `p000` as the proportion of disease-negative subjects with a negative test result to both tests. The covariance between test results for the disease-positive group is `p111 - se1 * se2`. The covariance between test results for the disease-negative group is `p000 - sp1 * sp2`.

References

Dohoo I, Martin W, Stryhn H (2003). Veterinary Epidemiologic Research. AVC Inc, Charlottetown, Prince Edward Island, Canada, pp. 47 and pp. 102 - 103.

Examples

```
## EXAMPLE 1:
## We would like to confirm the absence of disease in a single 1000-cow
## dairy herd. We expect the prevalence of disease in the herd to be 5%.
## We intend to use a single test with a sensitivity of 0.90 and a
## specificity of 0.80. How many samples should we take to be 95% certain
## that, if all tests are negative, the disease is not present?

epi.detectsize(N = 1000, prev = 0.05, se = 0.90, sp = 0.80, interpretation =
   "series", covar = c(0,0), conf.level = 0.95, finite.correction = TRUE)

## We need to sample 59 cows.

## EXAMPLE 2:
## We would like to confirm the absence of disease in a study area. If the
## disease is present we expect the between-herd prevalence to be 8% and the
## within-herd prevalence to be 5%. We intend to use two tests: the first has
## a sensitivity and specificity of 0.90 and 0.80, respectively. The second
## has a sensitivity and specificity of 0.95 and 0.85, respectively. The two
## tests will be interpreted in parallel. How many herds and cows within herds
## should we sample to be 95% certain that the disease is not present in the
## study area if all tests are negative? There area is comprised of
## approximately 5000 herds and the average number of cows per herd is 100.

epi.detectsize(N = c(5000, 100), prev = c(0.08, 0.05), se = c(0.90, 0.95),
   sp = c(0.80, 0.85), interpretation = "parallel", covar = c(0,0),
   conf.level = 0.95, finite.correction = TRUE)

## We need to sample 31 cows from 38 herds (a total of 1178 samples).
## The sensitivity of this testing regime is 99%. The specificity of this
## testing regime is 68%.

## EXAMPLE 3:
## You want to document the absence of Mycoplasma from a 200-sow pig herd.
## Based on your experience and the literature, a minimum of 20% of sows
```

```
## would have seroconverted if Mycoplasma were present in the herd. How many
## sows do you need to sample?

epi.detectsize(N = 200, prev = 0.20, se = 1.00, sp = 1.00, conf.level = 0.95,
   finite.correction = TRUE)

## If you test 12 sows and all test negative you can state that you are 95%
## confident that the prevalence rate of Mycoplasma in the herd is less than
## 20%.
```

`epi.dgamma` *Estimate the precision of a [structured] heterogeneity term*

Description

Returns the precision of a [structured] heterogeneity term after one has specified the amount of variation a priori.

Usage

```
epi.dgamma(rr, quantiles = c(0.05, 0.95))
```

Arguments

`rr`	the lower and upper limits of relative risk, estimated *a priori*.
`quantiles`	a vector of length two defining the quantiles of the lower and upper relative risk estimates.

Value

Returns the precision (the inverse variance) of the heterogeneity term.

References

Best, NG. WinBUGS 1.3.1 Short Course, Brisbane, November 2000.

Examples

```
## Suppose we are expecting the lower 5% and upper 95% confidence interval
## of relative risk in a data set to be 0.5 and 3.0, respectively.
## A prior guess at the precision of the heterogeneity term would be:

tau <- epi.dgamma(rr = c(0.5, 3.0), quantiles = c(0.05, 0.95))
tau

## This can be translated into a gamma distribution. We set the mean of the
## distribution as tau and specify a large variance (that is, we are not
## certain about tau).
```

```
mean <- tau
var <- 1000
shape <- mean^2 / var
inv.scale <- mean / var

## In WinBUGS the precision of the heterogeneity term may be parameterised
## as tau ~ dgamma(shape, inv.scale). Plot the probability density function
## of tau:

z <- seq(0.01, 10, by = 0.01)
fz <- dgamma(z, shape = shape, scale = 1/inv.scale)
plot(z, fz, type = "l", ylab = "Probability density of tau")
```

`epi.directadj` *Directly adjusted incidence rate estimates*

Description

Compute directly adjusted incidence rates.

Usage

```
epi.directadj(obs, tar, std, units = 1, conf.level = 0.95)
```

Arguments

`obs`	a matrix representing the observed number of events. Rows represent strata (e.g. region); columns represent the covariates to be adjusted for (e.g. age class, gender). The sum of each row will equal the total number of events for each stratum. The rows of the `obs` matrix must be named with the appropriate strata names. The columns of `obs` must be named with the appropriate level identifiers for the covariate. See the example, below.
`tar`	a matrix representing population time at risk. Rows represent strata (e.g. region); columns represent the covariates to be adjusted for (e.g. age class, gender). The sum of each row will equal the total population time at risk within each stratum. The rows of the `pop` matrix must be named with the appropriate strata names. The columns of `pop` must be named with the appropriate level identifiers for the covariate. See the example, below.
`std`	a matrix representing the standard population size for the different levels of the covariate to be adjusted for. The columns of `std` must be named with the appropriate level identifiers for the covariate(s).
`units`	multiplier for the incidence rate estimates.
`conf.level`	magnitude of the returned confidence interval. Must be a single number between 0 and 1.

Details

This function returns unadjusted (crude) and directly adjusted incidence rate estimates for each of the specified population strata. The term 'covariate' is used here to refer to the factors we want to control (i.e. adjust) for when calculating the directly adjusted incidence rate estimates.

When the outcome of interest is rare, the confidence intervals for the adjusted incidence rates returned by this function (based on Fay and Feuer, 1997) will be appropriate for incidence risk data. In this situation the argument `tar` is assumed to represent the size of the population at risk (instead of population time at risk). Example 3 (below) provides an approach if you are working with incidence risk data and the outcome of interest is not rare.

Value

A list containing the following:

`crude`	the crude incidence rate estimates for each stratum-covariate combination.
`crude.strata`	the crude incidence rate estimates for each stratum.
`adj.strata`	the directly adjusted incidence rate estimates for each stratum.

Author(s)

Thanks to Karl Ove Hufthammer for helpful suggestions to improve the execution and documentation of this function.

References

Fay M, Feuer E (1997). Confidence intervals for directly standardized rates: A method based on the gamma distribution. Statistics in Medicine 16: 791 - 801.

Fleiss JL (1981). Statistical Methods for Rates and Proportions, Wiley, New York, USA, pp. 240.

Frome E, Checkoway H (1985). Use of Poisson regression models in estimating incidence rates and ratios. American Journal of Epidemiology 121: 309 - 323.

Greenland S, Rothman KJ. Introduction to stratified analysis. In: Rothman KJ, Greenland S (1998). Modern Epidemiology. Lippincott Williams, & Wilkins, Philadelphia, pp. 260 - 265.

Thrusfield M (2007). Veterinary Epidemiology, Blackwell Publishing, London, UK, pp. 63 - 64.

Wilcosky T, Chambless L (1985). A comparison of direct adjustment and regression adjustment of epidemiologic measures. Journal of Chronic Diseases 38: 849 - 956.

See Also

`epi.indirectadj`

Examples

```
## EXAMPLE 1 (from Thrusfield 2007 pp. 63 - 64):
## A study was conducted to estimate the seroprevalence of leptospirosis
## in dogs in Glasgow and Edinburgh, Scotland. For the matrix titled pop
## the numbers represent dog-years at risk. The following data were
## obtained for male and female dogs:
```

```
dat <- data.frame(obs = c(15,46,53,16), tar = c(48,212,180,71),
   sex = c("M","F","M","F"), city = c("ED","ED","GL","GL"))

obs <- matrix(dat$obs, nrow = 2, byrow = TRUE,
   dimnames = list(c("ED","GL"), c("M","F")))
tar <- matrix(dat$tar, nrow = 2, byrow = TRUE,
   dimnames = list(c("ED","GL"), c("M","F")))
std <- matrix(data = c(250,250), nrow = 1, byrow = TRUE,
   dimnames = list("", c("M","F")))

## Compute directly adjusted seroprevalence estimates, using a standard
## population with equal numbers of male and female dogs:

std <- matrix(data = c(250,250), nrow = 1, byrow = TRUE,
   dimnames = list("", c("M","F")))

epi.directadj(obs, tar, std, units = 1, conf.level = 0.95)

## > $crude
## >   strata cov       est     lower     upper
## > 1     ED   M 0.3125000 0.1749039 0.5154212
## > 2     GL   M 0.2944444 0.2205591 0.3851406
## > 3     ED   F 0.2169811 0.1588575 0.2894224
## > 4     GL   F 0.2253521 0.1288082 0.3659577

## > $crude.strata
## >  strata       est     lower     upper
## > 1     ED 0.2346154 0.1794622 0.3013733
## > 2     GL 0.2749004 0.2138889 0.3479040

## > $adj.strata
## >   strata       est     lower     upper
## > 1     ED 0.2647406 0.1866047 0.3692766
## > 2     GL 0.2598983 0.1964162 0.3406224

## The confounding effect of gender has been removed by the adjusted
## incidence rate estimates.

## The adjusted incidence rate of leptospirosis in Glasgow dogs is 26 (95%
## CI 20 to 34) cases per 100 dog-years at risk.

## EXAMPLE 2 --- A more flexible approach for calculating adjusted incidence
## rate estimates using Poisson regression. See Frome and Checkoway (1985) for
## details.
dat.glm01 <- glm(obs ~ city, offset = log(tar), family = poisson, data = dat)
summary(dat.glm01)

## If you want to obtain adjusted incidence rate estimates, use the predict
## method on a new data set with the time at risk (tar) variable set to 1
## (which means log(tar) = 0). This will return the predicted number of
## cases per one unit of individual time, i.e. the incidence rate.
```

```
dat.pred01 <- predict(object = dat.glm01, newdata =
   data.frame(city = c("ED","GL"), tar = c(1,1)),
   type  = "link", se = TRUE)

conf.level <- 0.95
critval <- qnorm(p = 1 - ((1 - conf.level) / 2), mean = 0, sd = 1)
est <- dat.glm01$family$linkinv(dat.pred01$fit)
lower <- dat.glm01$family$linkinv(dat.pred01$fit -
   (critval * dat.pred01$se.fit))
upper <- dat.glm01$family$linkinv(dat.pred01$fit +
   (critval * dat.pred01$se.fit))
round(data.frame(est, lower, upper), 3)

##   est lower upper
## 0.235 0.183 0.302
## 0.275 0.217 0.348
## Results identical to the crude incidence rate estimates from
## epi.directadj.

## We now adjust for the effect of gender and city and report the adjusted
## incidence rate estimates for each city:
dat.glm02 <- dat.glm02 <- glm(obs ~ city + sex, offset = log(tar),
   family = poisson, data = dat)
dat.pred02 <- predict(object = dat.glm02, newdata =
   data.frame(sex = c("F","F"), city = c("ED","GL"), tar = c(1,1)),
   type  = "link", se.fit = TRUE)

conf.level <- 0.95
critval <- qnorm(p = 1 - ((1 - conf.level) / 2), mean = 0, sd = 1)
est <- dat.glm02$family$linkinv(dat.pred02$fit)
lower <- dat.glm02$family$linkinv(dat.pred02$fit -
   (critval * dat.pred02$se.fit))
upper <- dat.glm02$family$linkinv(dat.pred02$fit +
   (critval * dat.pred02$se.fit))
round(data.frame(est, lower, upper), 3)

##   est lower upper
## 0.220 0.168 0.287
## 0.217 0.146 0.323

## Using Poisson regression the gender adjusted incidence rate of leptospirosis
## in Glasgow dogs was 22 (95% CI 15 to 32) cases per 100 dog-years at risk.
## These results won't be the same as those using direct adjustment because
## for direct adjustment we use a contrived standard population.

## EXAMPLE 3 --- Logistic regression to return adjusted incidence risk
## estimates:

## Say, for argument's sake, that we are now working with incidence risk data.
## Here we'll re-label the variable 'tar' (time at risk) as 'pop'
## (population size). We adjust for the effect of gender and city and
## report the adjusted incidence risk of canine leptospirosis estimates for
## each city:
```

```
dat$pop <- dat$tar

dat.glm03 <- glm(cbind(obs, pop - obs) ~ city + sex,
   family = "binomial", data = dat)
dat.pred03 <- predict(object = dat.glm03, newdata =
   data.frame(sex = c("F","F"), city = c("ED","GL")),
   type  = "link", se.fit = TRUE)

conf.level <- 0.95
critval <- qnorm(p = 1 - ((1 - conf.level) / 2), mean = 0, sd = 1)
est <- dat.glm03$family$linkinv(dat.pred03$fit)
lower <- dat.glm03$family$linkinv(dat.pred03$fit -
   (critval * dat.pred03$se.fit))
upper <- dat.glm03$family$linkinv(dat.pred03$fit +
   (critval * dat.pred03$se.fit))
round(data.frame(est, lower, upper), 3)

##   est lower upper
## 0.220 0.172 0.276
## 0.217 0.150 0.304

## The adjusted incidence risk of leptospirosis in Glasgow dogs is 22 (95%
## CI 15 to 30) cases per 100 dogs at risk.
```

---

epi.dms *Decimal degrees and degrees, minutes and seconds conversion*

Description

Converts decimal degrees to degrees, minutes and seconds. Converts degrees, minutes and seconds to decimal degrees.

Usage

```
epi.dms(dat)
```

Arguments

dat	the data. A one-column matrix is assumed when converting decimal degrees to degrees, minutes, and seconds. A two-column matrix is assumed when converting degrees and decimal minutes to decimal degrees. A three-column matrix is assumed when converting degrees, minutes and seconds to decimal degrees.

Examples

```
## EXAMPLE 1:
## Degrees, minutes, seconds to decimal degrees:
dat <- matrix(c(41, 38, 7.836, -40, 40, 27.921),
```

```
   byrow = TRUE, nrow = 2)
epi.dms(dat)

## EXAMPLE 2:
## Decimal degrees to degrees, minutes, seconds:
dat <- matrix(c(41.63551, -40.67442), nrow = 2)
epi.dms(dat)
```

`epi.dsl` *Mixed-effects meta-analysis of binary outcomes using the DerSimonian and Laird method*

Description

Computes individual study odds or risk ratios for binary outcome data. Computes the summary odds or risk ratio using the DerSimonian and Laird method. Performs a test of heterogeneity among trials. Performs a test for the overall difference between groups (that is, after pooling the studies, do treated groups differ significantly from controls?).

Usage

```
epi.dsl(ev.trt, n.trt, ev.ctrl, n.ctrl, names, method = "odds.ratio",
   alternative = c("two.sided", "less", "greater"), conf.level = 0.95)
```

Arguments

`ev.trt`	observed number of events in the treatment group.
`n.trt`	number in the treatment group.
`ev.ctrl`	observed number of events in the control group.
`n.ctrl`	number in the control group.
`names`	character string identifying each trial.
`method`	a character string indicating the method to be used. Options are `odds.ratio` or `risk.ratio`.
`alternative`	a character string specifying the alternative hypothesis, must be one of `two.sided`, `greater` or `less`.
`conf.level`	magnitude of the returned confidence interval. Must be a single number between 0 and 1.

Details

`alternative = "greater"` tests the hypothesis that the DerSimonian and Laird summary measure of association is greater than 1.

Value

A list containing the following:

OR	the odds ratio for each trial and the lower and upper bounds of the confidence interval of the odds ratio for each trial.
RR	the risk ratio for each trial and the lower and upper bounds of the confidence interval of the risk ratio for each trial.
OR.summary	the DerSimonian and Laird summary odds ratio and the lower and upper bounds of the confidence interval of the DerSimonian and Laird summary odds ratio.
RR.summary	the DerSimonian and Laird summary risk ratio and the lower and upper bounds of the confidence interval of the DerSimonian and Laird summary risk ratio.
weights	the inverse variance and DerSimonian and Laird weights for each trial.
heterogeneity	a vector containing Q the heterogeneity test statistic, df the degrees of freedom and its associated P-value.
Hsq	the relative excess of the heterogeneity test statistic Q over the degrees of freedom df.
Isq	the percentage of total variation in study estimates that is due to heterogeneity rather than chance.
tau.sq	the variance of the treatment effect among trials.
effect	a vector containing z the test statistic for overall treatment effect and its associated P-value.

Note

Under the random-effects model, the assumption of a common treatment effect is relaxed, and the effect sizes are assumed to have a normal distribution with variance tau.sq.

Using this method, the DerSimonian and Laird weights are used to compute the pooled odds ratio.

The function checks each strata for cells with zero frequencies. If a zero frequency is found in any cell, 0.5 is added to all cells within the strata.

References

Deeks JJ, Altman DG, Bradburn MJ (2001). Statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. In: Egger M, Davey Smith G, Altman D (eds). Systematic Review in Health Care Meta-Analysis in Context. British Medical Journal, London, 2001, pp. 291 - 299.

DerSimonian R, Laird N (1986). Meta-analysis in clinical trials. Controlled Clinical Trials 7: 177 - 188.

Higgins J, Thompson S (2002). Quantifying heterogeneity in a meta-analysis. Statistics in Medicine 21: 1539 - 1558.

See Also

epi.iv, epi.mh, epi.smd

Examples

```
data(epi.epidural)
epi.dsl(ev.trt = epi.epidural$ev.trt, n.trt = epi.epidural$n.trt,
   ev.ctrl = epi.epidural$ev.ctrl, n.ctrl = epi.epidural$n.ctrl,
   names = as.character(epi.epidural$trial), method = "odds.ratio",
   alternative = "two.sided", conf.level = 0.95)
```

---

epi.edr *Estimated dissemination ratio*

Description

Computes estimated dissemination ratio on the basis of a vector of numbers (usually counts of incident cases identified on each day of an epidemic).

Usage

```
epi.edr(dat, n = 4, conf.level = 0.95, nsim = 99, na.zero = TRUE)
```

Arguments

`dat`	a numeric vector listing the number of incident cases for each day of an epidemic.
`n`	scalar, defining the number of days to be used when computing the estimated dissemination ratio.
`conf.level`	magnitude of the returned confidence interval. Must be a single number between 0 and 1.
`nsim`	scalar, defining the number of simulations to be used for the confidence interval calculations.
`na.zero`	logical, replace `NaN` or `Inf` values with zeros?

Details

In infectious disease epidemics the *n*-day estimated dissemination ratio (EDR) at day *i* equals the total number of incident cases between day `i` and day `[i - (n - 1)]` (inclusive) divided by the total number of incident cases between day `(i - n)` and day `(i - 2n) + 1` (inclusive). EDR values are often calculated for each day of an epidemic and presented as a time series analysis. If the EDR is consistently less than unity, the epidemic is said to be 'under control'.

A simulation approach is used to calculate confidence intervals around each daily EDR estimate. The numerator and denominator of the EDR estimate for each day is taken in turn and a random number drawn from a Poisson distribution, using the calculated numerator and denominator value as the mean. EDR is then calculated for these simulated values and the process repeated `nsim` times. Confidence intervals are then derived from the vector of simulated values for each day.

Value

Returns the point estimate of the EDR and the lower and upper bounds of the confidence interval of the EDR.

References

Miller W (1976). A state-transition model of epidemic foot-and-mouth disease. In: Proceedings of an International Symposium: New Techniques in Veterinary Epidemiology and Economics, University of Reading, Reading, pp. 56 - 72.

Morris R, Sanson R, Stern M, Stevenson M, Wilesmith J (2002). Decision-support tools for foot-and-mouth disease control. Revue Scientifique et Technique de l'Office International des Epizooties 21, 557 - 567.

Examples

```
set.seed(123)
dat <- rpois(n = 50, lambda = 2)
edr.04 <- epi.edr(dat, n = 4, conf.level = 0.95, nsim = 99, na.zero = TRUE)
sdate <- as.Date(x = "31/12/2015", format = "%d/%m/%Y")

dat.04 <- data.frame(idate = sdate + 1:50, est = edr.04$est,
   low = edr.04$lower, upp = edr.04$upper)

## Line plot of EDR (and its 95% confidence interval) as a function of
## calendar time:

## Not run:
library(ggplot2)

ggplot(dat.04, aes(x = as.integer(idate), y = est)) +
   geom_line() +
   geom_line(dat = dat.04, aes(x = as.integer(idate), y = upp),
      lty = 3, size = 0.5) +
   geom_line(dat = dat.04, aes(x = as.integer(idate), y = low),
      lty = 3, size = 0.5) +
   scale_x_continuous(name = "Date",
      breaks = seq(from = min(as.integer(dat.04$idate)),
         to = max(as.integer(dat.04$idate)), by = 7),
      labels = seq(from = min(dat.04$idate),
         to = max(dat.04$idate), by = 7),
      limits = c(min(as.integer(dat.04$idate)),
         max(as.integer(dat.04$idate)))) +
   scale_y_continuous(name = "Estimated disemination ratio (EDR)",
   limits = c(0,10)) +
   theme(axis.text.x = element_text(angle = 90, vjust = 0.5, size = 10)) +
   geom_hline(yintercept = 1, lty = 2)

## End(Not run)
```

`epi.empbayes` *Empirical Bayes estimates*

Description

Computes empirical Bayes estimates of observed event counts using the method of moments.

Usage

```
epi.empbayes(obs, pop)
```

Arguments

`obs`	a vector representing the observed event counts in each unit of interest.
`pop`	a vector representing the population count in each unit of interest.

Details

The gamma distribution is parameterised in terms of shape (α) and scale (ν) parameters. The mean of a given gamma distribution equals ν/α. The variance equals ν/α^2. The empirical Bayes estimate of event risk in each unit of interest equals $(obs + \nu)/(pop + \alpha)$.

This technique performs poorly when your data contains large numbers of zero event counts. In this situation a Bayesian approach for estimating α and ν would be advised.

Value

A data frame with four elements: `gamma` the mean event risk across all units, `phi` the variance of event risk across all units, `alpha` the estimated shape parameter of the gamma distribution, and `nu` the estimated scale parameter of the gamma distribution.

References

Bailey TC, Gatrell AC (1995). Interactive Spatial Data Analysis. Longman Scientific & Technical. London, pp. 303 - 308.

Langford IH (1994). Using empirical Bayes estimates in the geographical analysis of disease risk. Area 26: 142 - 149.

Meza J (2003). Empirical Bayes estimation smoothing of relative risks in disease mapping. Journal of Statistical Planning and Inference 112: 43 - 62.

Examples

```
data(epi.SClip)
obs <- epi.SClip$cases; pop <- epi.SClip$population

est <- epi.empbayes(obs, pop)
crude.p <- ((obs) / (pop)) * 100000
crude.r <- rank(crude.p)
```

```
ebay.p <- ((obs + est[4]) / (pop + est[3])) * 100000
dat <- data.frame(rank = c(crude.r, crude.r),
   Method = c(rep("Crude", times = length(crude.r)),
      rep("Empirical Bayes", times = length(crude.r))),
   est = c(crude.p, ebay.p))

## Scatter plot showing the crude and empirical Bayes adjusted lip cancer
## incidence rates as a function of district rank for the crude lip
## cancer incidence rates:

## Not run:
library(ggplot2)

ggplot(dat, aes(x = rank, y = est, colour = Method)) +
   geom_point() +
   ylab("Lip cancer incidence rates (cases per 100,000 person years)") +
   scale_x_continuous(name = "District rank",
      breaks = seq(from = 0, to = 60, by = 10),
      labels = seq(from = 0, to = 60, by = 10),
      limits = c(0,60)) +
   ylim(0,30)

## End(Not run)
```

---

epi.epidural *Rates of use of epidural anaesthesia in trials of caregiver support*

Description

This data set provides results of six trials investigating rates of use of epidural anaesthesia during childbirth. Each trial is made up of a group where a caregiver (midwife, nurse) provided support intervention and a group where standard care was provided. The objective was to determine if there were higher rates of epidural use when a caregiver was present at birth.

Usage

```
data(epi.epidural)
```

Format

A data frame with 6 observations on the following 5 variables.

trial the name and year of the trial.

ev.trt number of births in the caregiver group where an epidural was used.

n.trt number of births in the caregiver group.

ev.ctrl number of births in the standard care group where an epidural was used.

n.ctrl number of births in the standard care group.

References

Deeks JJ, Altman DG, Bradburn MJ (2001). Statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. In: Egger M, Davey Smith G, Altman D (eds). Systematic Review in Health Care Meta-Analysis in Context. British Medical Journal, London, pp. 291 - 299.

`epi.equivb` *Estimate the sample size for a parallel equivalence trial, binary outcomes*

Description

Computes the sample size for a parallel equivalence trial with a binary outcome variable.

Usage

```
epi.equivb(treat, control, delta, n, r = 1, power, alpha)
```

Arguments

`treat`	the expected proportion of successes in the treatment group.
`control`	the expected proportion of successes in the control group.
`delta`	the equivalence limit, expressed as a proportion.
`n`	scalar, the total number of study subjects in the trial.
`r`	scalar, the number in the treatment group divided by the number in the control group.
`power`	scalar, the required study power.
`alpha`	scalar, defining the desired alpha level.

Value

A list containing one or more of the following:

`n.treat`	the required number of study subject in the treatment group.
`n.control`	the required number of study subject in the control group.
`n.total`	the total number of study subjects required.

Note

Consider a clinical trial comparing two groups, a standard treatment (s) and a new treatment (n). In each group, a proportion of subjects respond to the treatment: Ps and Pn.

With a superiority trial we specify the maximum acceptable difference between Pn and Ps as `delta`. The null hypothesis is H0: Pn - Ps <= `delta` and the alternative hypothesis is H1: Pn - Ps > `delta`.

An equivalence trial is used if want to prove that two treatments produce the same clinical outcomes. With an equivalence trial, we specify the maximum acceptable difference between Pn and Ps as `delta`. The null hypothesis is H0: |Ps - Pn| >= `delta` and the alternative hypothesis is H1: |Ps - Pn| < `delta`. In bioequivalence trials, a 90% confidence interval is often used. The value of the maximum acceptable difference `delta` is chosen so that a patient will not detect any change in effect when replacing the standard treatment with the new treatment.

With a non-inferiority trial, we specify the maximum acceptable difference between Pn and Ps as `delta`. The null hypothesis is H0: Ps - Pn >= `delta` and the alternative hypothesis is H1: Ps - Pn < `delta`. The aim of a non-inferiority trial is show that a new treatment is not (much) inferior to a standard treatment. Showing non-inferiority can be of interest because: (a) it is often not ethically possible to do a placebo-controlled trial, (b) the new treatment is not expected to be better than the standard treatment on primary efficacy endpoints, but is safer, (c) the new treatment is not expected to be better than the standard treatment on primary efficacy endpoints, but is cheaper to produce or easier to administer, (d) the new treatment is not expected to be better than the standard treatment on primary efficacy endpoints in clinical trial, but compliance will be better outside the clinical trial and hence efficacy better outside the trial.

To summarise (adapted from Machin et al. 2009, page 105):

Test for	Null hypothesis	Alt hypothesis	Type I	Type II
Superiority	H0: Pn - Ps <= delta	H1: Pn - Ps > delta	2 sided, 5.0%	1 sided, 10 or 20%
Equivalence	H0: |Pn - Ps| >= delta	H1: |Pn - Ps| < delta	1 sided, 5.0%	1 sided, 20%
Non-inferiority	H0: Pn - Ps >= delta	H1: Pn - Ps < delta	1 sided, 2.5%	1 sided, 10 or 20%

Superiority trial: H1 is that the new treatment is better than the standard treatment.
Equivalence trial: H1 is that the new treatment is not too different from the standard treatment.
Non-inferiority trial: H1 is that the new treatment is not much worse than the standard treatment.

When calculating the power of a study, note that the variable `n` refers to the total study size (that is, the number of subjects in the treatment group plus the number in the control group).

References

Chow S, Shao J, Wang H (2008). Sample Size Calculations in Clinical Research. Chapman & Hall/CRC Biostatistics Series, pp. 91.

Ewald B (2013). Making sense of equivalence and non-inferiority trials. Australian Prescriber 36: 170 - 173.

Julious SA (2004). Sample sizes for clinical trials with normal data. Statistics in Medicine 23: 1921 - 1986.

Julious SA (2009). Estimating Samples Sizes in Clinical Trials. CRC, New York.

Machin D, Campbell MJ, Tan SB, Tan SH (2009). Sample Size Tables for Clinical Studies. Wiley Blackwell, New York.

Examples

```
## EXAMPLE 1 (from Machin, Campbell, Tan and Tan 2009 p. 113):
## Bennett, Dismukes, Duma et al. (1979) designed a clinical trial to test
## whether combination chemotherapy for a shorter period would be at least
## as good as conventional therapy for patients with cryptococcal meningitis.
## They recruited 39 patients to each treatment arm and wished to conclude
## that a difference of less than 20% in response rate between the treatments
## would indicate equivalence. Assuming a one-sided test size of 10%, a
## power of 80% and an overall response rate of 50%, what would be a
## realistic sample size if the trial were to be repeated?

epi.equivb(treat = 0.50, control = 0.50, delta = 0.20, n = NA, r = 1,
   power = 0.80, alpha = 0.10)

## A total of 166 subjects need to be enrolled in the trial, 83 in the
## treatment group and 83 in the control group.
```

---

epi.equivc *Estimate the sample size for a parallel equivalence trial, continuous outcomes*

Description

Computes the sample size for a parallel equivalence trial with a continuous outcome variable.

Usage

```
epi.equivc(treat, control, sd, delta, n, r = 1, power, alpha)
```

Arguments

treat	the expected mean of the outcome of interest in the treatment group.
control	the expected mean of the outcome of interest in the control group.
sd	the expected population standard deviation of the outcome of interest.
delta	the equivalence limit, expressed as a proportion.
n	scalar, the total number of study subjects in the trial.
r	scalar, the number in the treatment group divided by the number in the control group.
power	scalar, the required study power.
alpha	scalar, defining the desired alpha level.

Value

A list containing one or more of the following:

n.treat	the required number of study subject in the treatment group.
n.control	the required number of study subject in the control group.
n.total	the total number of study subjects required.

Note

Consider a clinical trial comparing two groups, a standard treatment (s) and a new treatment (n). In each group, a proportion of subjects respond to the treatment: Ps and Pn.

With a superiority trial we specify the maximum acceptable difference between Pn and Ps as delta. The null hypothesis is H0: Pn - Ps <= delta and the alternative hypothesis is H1: Pn - Ps > delta.

An equivalence trial is used if want to prove that two treatments produce the same clinical outcomes. With an equivalence trial, we specify the maximum acceptable difference between Pn and Ps as delta. The null hypothesis is H0: |Ps - Pn| >= delta and the alternative hypothesis is H1: |Ps - Pn| < delta. In bioequivalence trials, a 90% confidence interval is often used. The value of the maximum acceptable difference delta is chosen so that a patient will not detect any change in effect when replacing the standard treatment with the new treatment.

With a non-inferiority trial, we specify the maximum acceptable difference between Pn and Ps as delta. The null hypothesis is H0: Ps - Pn >= delta and the alternative hypothesis is H1: Ps - Pn < delta. The aim of a non-inferiority trial is show that a new treatment is not (much) inferior to a standard treatment. Showing non-inferiority can be of interest because: (a) it is often not ethically possible to do a placebo-controlled trial, (b) the new treatment is not expected to be better than the standard treatment on primary efficacy endpoints, but is safer, (c) the new treatment is not expected to be better than the standard treatment on primary efficacy endpoints, but is cheaper to produce or easier to administer, (d) the new treatment is not expected to be better than the standard treatment on primary efficacy endpoints in clinical trial, but compliance will be better outside the clinical trial and hence efficacy better outside the trial.

For a summary of the key features of superiority, equivalence and non-inferiority trials, refer to the documentation for epi.equivb.

When calculating the power of a study, note that the variable n refers to the total study size (that is, the number of subjects in the treatment group plus the number in the control group).

References

Bennett JE, Dismukes WE, Duma RJ, Medoff G, Sande MA, Gallis H, Leonard J, Fields BT, Bradshaw M, Haywood H, McGee Z, Cate TR, Cobbs CG, Warner JF and Alling DW (1979). A comparison of amphotericin B alone and combined flucytosine in the treatment of cryptococcal meningitis. New England Journal of Medicine 301: 126 - 131.

Chow S, Shao J, Wang H (2008). Sample Size Calculations in Clinical Research. Chapman & Hall/CRC Biostatistics Series, pp. 91.

Ewald B (2013). Making sense of equivalence and non-inferiority trials. Australian Prescriber 36: 170 - 173.

Julious SA (2004). Sample sizes for clinical trials with normal data. Statistics in Medicine 23: 1921 - 1986.

Julious SA (2009). Estimating Samples Sizes in Clinical Trials. CRC, New York.

Machin D, Campbell MJ, Tan SB, Tan SH (2009). Sample Size Tables for Clinical Studies. Wiley Blackwell, New York.

Examples

```
## EXAMPLE 1 (from Machin, Campbell, Tan and Tan 2009 p. 113):
## It is anticipated that patients on a particular drug have a mean diastolic
## blood pressure of 96 mmHg, as against 94 mmHg on an alternative. It is also
## anticipated that the standard deviation of diastolic BP is approximately
## 8 mmHg. If one wishes to confirm that the difference is likely to be less
## than 5 mmHg, that is, one wishes to show equivalence, how many patients
## are need to be enrolled in the trial? Assume 80% power and
## 95% significance.

epi.equivc(treat = 94, control = 96, sd = 8, delta = 5, n = NA,
   r = 1, power = 0.80, alpha = 0.05)

## A total of 244 subjects need to be enrolled in the trial, 122 in the
## treatment group and 122 in the control group.

## EXAMPLE 2 (from Chow S, Shao J, Wang H 2008, p. 64):
## A pharmaceutical company is interested in conducting a clinical trial
## to compare two cholesterol lowering agents for treatment of patients with
## congestive heart disease using a parallel design. The primary efficacy
## parameter is the LDL. In what follows, we will consider the situation
## where the intended trial is for testing equivalence of mean responses
## in LDL. Assume that 80% power is required at a 5% level of significance.

## In this example, we assume a 5 unit (i.e. delta = 5) change of LDL is
## considered of clinically meaningful difference. Assume the standard
## of LDL is 10 units and the LDL concentration in the treatment group is 20
## units and the LDL concentration in the control group is 21 units.

epi.equivc(treat = 20, control = 21, sd = 10, delta = 5, n = NA,
   r = 1, power = 0.80, alpha = 0.05)

## A total of 216 subjects need to be enrolled in the trial, 108 in the
## treatment group and 108 in the control group.

## EXAMPLE 2 (cont.):
## Suppose only 150 subjects were enrolled in the trial, 75 in the treatment
## group and 75 in the control group. What is the estimated study power?

epi.equivc(treat = 0.20, control = 0.21, sd = 0.10, delta = 0.05, n = 150,
   r = 1, power = NA, alpha = 0.05)

## With only 150 subjects the estimated study power is 0.58.
```

epi.herdtest *Estimate herd test characteristics*

Description

When tests are applied to individuals within a group we may wish to designate the group as being either diseased or non-diseased on the basis of the individual test results. This function estimates sensitivity and specificity of this testing regime at the group (or herd) level.

Usage

```
epi.herdtest(se, sp, P, N, n, k)
```

Arguments

se	a vector of length one defining the sensitivity of the individual test used.
sp	a vector of length one defining the specificity of the individual test used.
P	scalar, defining the estimated true prevalence.
N	scalar, defining the herd size.
n	scalar, defining the number of individuals to be tested per group (or herd).
k	scalar, defining the critical number of individuals testing positive that will denote the group as test positive.

Value

A data frame with four elements: APpos the probability of obtaining a positive test, APneg the probability of obtaining a negative test, HSe the estimated group (herd) sensitivity, and HSp the estimated group (herd) specificity.

Note

The method implemented in this function is based on the hypergeometric distribution.

Author(s)

Ron Thornton, MAF New Zealand, PO Box 2526 Wellington, New Zealand.

References

Dohoo I, Martin W, Stryhn H (2003). Veterinary Epidemiologic Research. AVC Inc, Charlottetown, Prince Edward Island, Canada, pp. 113 - 115.

Examples

```
## EXAMPLE 1:
## We wish to estimate the herd-level sensitivity and specificity of
## a testing regime using an individual animal test of sensitivity 0.391
## and specificity 0.964. The estimated true prevalence of disease is 0.12.
## Assume that 60 individuals will be tested per herd and we have
## specified that two or more positive test results identify the herd
## as positive.

epi.herdtest(se = 0.391, sp = 0.964, P = 0.12, N = 1E06, n = 60, k = 2)

## This testing regime gives a herd sensitivity of 0.95 and a herd
## specificity of 0.36. With a herd sensitivity of 0.95 we can be
## confident that we will declare a herd infected if it is infected.
## With a herd specficity of only 0.36, we will declare 0.64 of disease
## negative herds as infected, so false positives are a problem.
```

---

epi.incin *Laryngeal and lung cancer cases in Lancashire 1974 - 1983*

Description

Between 1972 and 1980 an industrial waste incinerator operated at a site about 2 kilometres south-west of the town of Coppull in Lancashire, England. Addressing community concerns that there were greater than expected numbers of laryngeal cancer cases in close proximity to the incinerator Diggle et al. (1990) conducted a study investigating risks for laryngeal cancer, using recorded cases of lung cancer as controls. The study area is 20 km x 20 km in size and includes location of residence of patients diagnosed with each cancer type from 1974 to 1983. The site of the incinerator was at easting 354500 and northing 413600.

Usage

```
data(epi.incin)
```

Format

A data frame with 974 observations on the following 3 variables.

xcoord easting coordinate (in metres) of each residence.

ycoord northin coordinate (in metres) of each residence.

status disease status: 0 = lung cancer, 1 = laryngeal cancer.

Source

Bailey TC and Gatrell AC (1995). Interactive Spatial Data Analysis. Longman Scientific & Technical. London.

References

Diggle P, Gatrell A, and Lovett A (1990). Modelling the prevalence of cancer of the larynx in Lancashire: A new method for spatial epidemiology. In: Thomas R (Editor), Spatial Epidemiology. Pion Limited, London, pp. 35 - 47.

Diggle P (1990). A point process modelling approach to raised incidence of a rare phenomenon in the viscinity of a prespecified point. Journal of the Royal Statistical Society A 153: 349 - 362.

Diggle P, Rowlingson B (1994). A conditional approach to point process modelling of elevated risk. Journal of the Royal Statistical Society A 157: 433 - 440.

`epi.indirectadj` *Indirectly adjusted incidence risk estimates*

Description

Compute indirectly adjusted incidence risks and standardised mortality (incidence) ratios.

Usage

```
epi.indirectadj(obs, pop, std, units, conf.level = 0.95)
```

Arguments

`obs`	a one column matrix representing the number of observed number of events in each strata. The dimensions of `obs` must be named (see the examples, below).
`pop`	a matrix representing population size. Rows represent strata (e.g. region); columns represent the levels of the covariate to be adjusted for (e.g. age class, gender). The sum of each row will equal the total population size within each stratum. If there are no covariates `pop` will be a one column matrix. The dimensions of the `pop` matrix must be named (see the examples, below).
`std`	a one row matrix specifying the standard incidence risks to be applied to each level of the covariate to be adjusted for. The length of `std` should be one plus the number of covariates to be adjusted for (the additional value represents the incidence risk in the entire population). If there are no covariates to adjust for `std` is a single number representing the incidence risk in the entire population.
`units`	multiplier for the incidence risk estimates.
`conf.level`	magnitude of the returned confidence interval. Must be a single number between 0 and 1.

Details

Indirect standardisation can be performed whenever the stratum-specific incidence risk estimatesare either unknown or unreliable. If the stratum-specific incidence risk estimates are known, direct standardisation is preferred.

Confidence intervals for the standardised mortality ratio estimates are based on the Poisson distribution (see Breslow and Day 1987, p 69 - 71 for details).

Value

A list containing the following:

crude.strata	the crude incidence risk estimates for each stratum.
adj.strata	the indirectly adjusted incidence risk estimates for each stratum.
smr	the standardised mortality (incidence) ratios for each stratum.

Author(s)

Thanks to Dr. Telmo Nunes (UISEE/DETSA, Faculdade de Medicina Veterinaria - UTL, Rua Prof. Cid dos Santos, 1300-477 Lisboa Portugal) for details and code for the confidence interval calculations.

References

Breslow NE, Day NE (1987). Statistical Methods in Cancer Reasearch: Volume II - The Design and Analysis of Cohort Studies. Lyon: International Agency for Cancer Research.

Dohoo I, Martin W, Stryhn H (2009). Veterinary Epidemiologic Research. AVC Inc, Charlottetown, Prince Edward Island, Canada, pp. 85 - 89.

Rothman KJ, Greenland S (1998). Modern Epidemiology, second edition. Lippincott Williams & Wilkins, Philadelphia.

Sahai H, Khurshid A (1993). Confidence intervals for the mean of a Poisson distribution: A review. Biometrical Journal 35: 857 - 867.

Sahai H, Khurshid A (1996). Statistics in Epidemiology. Methods, Techniques and Applications. CRC Press, Baton Roca.

See Also

epi.directadj

Examples

```
## EXAMPLE 1 (without covariates):
## Adapted from Dohoo, Martin and Stryhn (2009). In this example the frequency
## of tuberculosis is expressed as incidence risk (i.e. the number of
## tuberculosis positive herds divided by the size of the herd population at
## risk). In their text, Dohoo et al. present the data as incidence rate (the
## number of tuberculosis positive herds per herd-year at risk).

## Data have been collected on the incidence of tuberculosis in two
## areas ("A" and "B"). Provided are the counts of (new) incident cases and
## counts of the herd population at risk. The standard incidence risk for
## the total population is 0.060 (6 cases per 100 herds at risk):

obs <- matrix(data = c(58, 130), nrow = 2, byrow = TRUE,
   dimnames = list(c("A", "B"), ""))
pop <- matrix(data = c(1000, 2000), nrow = 2, byrow = TRUE,
   dimnames = list(c("A", "B"), ""))
std <- 0.060
```

```
epi.indirectadj(obs = obs, pop = pop, std = std, units = 100,
   conf.level = 0.95)

## EXAMPLE 2 (with covariates):
## We now have, for each area, data stratified by herd type (dairy, beef).
## The standard incidence risks for beef herds, dairy herds, and the total
## population are 0.025, 0.085, and 0.060 cases per herd, respectively:

obs <- matrix(data = c(58, 130), nrow = 2, byrow = TRUE,
   dimnames = list(c("A", "B"), ""))
pop <- matrix(data = c(550, 450, 500, 1500), nrow = 2, byrow = TRUE,
   dimnames = list(c("A", "B"), c("Beef", "Dairy")))
std <- matrix(data = c(0.025, 0.085, 0.060), nrow = 1, byrow = TRUE,
   dimnames = list("", c("Beef", "Dairy", "Total")))

epi.indirectadj(obs = obs, pop = pop, std = std, units = 100,
   conf.level = 0.95)

## > $crude.strata
## >   est    lower    upper
## > A 5.8 4.404183 7.497845
## > B 6.5 5.430733 7.718222

## > $adj.strata
## >        est    lower    upper
## > A 6.692308 5.076923 8.423077
## > B 5.571429 4.628571 6.557143

## > $smr.strata
## >   obs exp       est     lower    upper
## > A  58  52 1.1153846 0.8461538 1.403846
## > B 130 140 0.9285714 0.7714286 1.092857

## The crude incidence risk of tuberculosis in area A was 5.8
## (95% CI 4.0 to 7.5) cases per 100 herds at risk. The crude incidence
## risk of tuberculosis in area B was 6.5 (95% CI 5.4 to 7.7) cases
## per 100 herds at risk.

## The indirectly adjusted incidence risk of tuberculosis in area A was 6.7
## (95% CI 5.1 to 8.4) cases per 100 herds at risk. The indirectly
## adjusted incidence risk of tuberculosis in area B was 5.6
## (95% CI 4.6 to 6.6) cases per 100 herds at risk.
```

`epi.insthaz` *Instantaneous hazard computed on the basis of a Kaplan-Meier survival function*

Description

Compute the instantaneous hazard on the basis of a Kaplan-Meier survival function.

Usage

```
epi.insthaz(survfit.obj, conf.level = 0.95)
```

Arguments

survfit.obj	a survfit object, computed using the survival package.
conf.level	magnitude of the returned confidence interval. Must be a single number between 0 and 1.

Details

Computes the instantaneous hazard of failure, equivalent to the proportion of the population failing per unit time.

Value

A data frame with three elements: time the observed failure times, est the proportion of the population failing per unit time, lower the lower bounds of the confidence interval, and upper the upper bounds of the confidence interval.

References

Venables W, Ripley B (2002). Modern Applied Statistics with S, fourth edition. Springer, New York, pp. 353 - 385.

Singer J, Willett J (2003). Applied Longitudinal Data Analysis Modeling Change and Event Occurrence. Oxford University Press, London, pp. 348.

Examples

```
require(survival)

ov.km <- survfit(Surv(futime, fustat) ~ 1, data = ovarian)
ov.haz <- epi.insthaz(ov.km, conf.level = 0.95)
ov.shaz <- data.frame(
   time = lowess(ov.haz$time, ov.haz$lower, f = 0.50)$x,
   est =  lowess(ov.haz$time, ov.haz$est, f = 0.50)$y,
   low =  lowess(ov.haz$time, ov.haz$lower, f = 0.50)$y,
   upp =  lowess(ov.haz$time, ov.haz$upper, f = 0.50)$y)

plot(x = ov.haz$time, y = ov.haz$est, xlab = "Days",
  ylab = "Instantaneous hazard", type = "b", pch = 16, ylim = c(0, 0.02))
lines(x = ov.shaz$time, y = ov.shaz$est,
   lty = 1, lwd = 2, col = "red")
lines(x = ov.shaz$time, y = ov.shaz$low,
   lty = 2, lwd = 1, col = "red")
lines(x = ov.shaz$time, y = ov.shaz$upp,
```

```
   lty = 2, lwd = 1, col = "red")

## Not run:
library(ggplot2)

ggplot(data = ov.haz, aes(x = time, y = est)) +
   geom_line() +
   geom_line(data = ov.shaz, aes(x = time, y = est),
      lty = 1, lwd = 1.0, col = "red") +
   geom_line(data = ov.shaz, aes(x = time, y = low),
      lty = 2, lwd = 0.5, col = "red") +
   geom_line(data = ov.shaz, aes(x = time, y = upp),
      lty = 2, lwd = 0.5, col = "red") +
   xlab(label = "Days") +
   ylab("Instantaneous hazard") +
   ylim(0, 0.02)

## End(Not run)
```

`epi.interaction` *Relative excess risk due to interaction in a case-control study*

Description

Computes the relative excess risk due to interaction, the proportion of disease among those with both exposures attributable to interaction, and the synergy index for case-control data. Confidence interval calculations are based on the delta method described by Hosmer and Lemeshow (1992).

Usage

```
epi.interaction(model, coeff, type = c("RERI", "APAB", "S"), conf.level = 0.95)
```

Arguments

`model`	an object of class `glm`, `clogit` or `coxph`.
`coeff`	a vector specifying the position of the two coefficients of their interaction term in the model.
`type`	character string defining the type of analysis to be run. Options are `RERI` the relative excess risk due to interaction, `APAB` the proportion of disease among those with both exposures that is attributable to interaction of the two exposures, and `S` the synergy index.
`conf.level`	magnitude of the returned confidence interval. Must be a single number between 0 and 1.

Details

Interaction is defined as a departure from additivity of effects in epidemiologic studies. This function calculates three indices defined by Rothman (1998): (1) the relative excess risk due to interaction (RERI), (2) the proportion of disease among those with both exposures that is attributable to their interaction (AP[AB]), and (3) the synergy index (S). The synergy index measures the interaction between two risk factors expressed as the ratio of the relative excess risk for the combined effect of the risk factors and the sum of the relative excess risks for each separate effect of the two risk factors. In the absence of interaction both RERI and AP[AB] = 0 and S = 1.

This function uses the delta method to calculate the confidence intervals for each of the interaction measures, as described by Hosmer and Lemeshow (1992). An error will be returned if the point estimate of the synergy index is less than one. In this situation a warning is issued advising the user to re-parameterise their model as a linear odds model. See Skrondal (2003) for further details.

RERI, APAB and S can be used to assess additive interaction when the odds ratio estimates the risk ratio. However, it is recognised that odds ratios from case-control studies are not designed to directly estimate the risk or rate ratio (and only do so well when the outcome of interest is rare).

Value

A data frame listing:

`est`	the point estimate of the requested interaction measure.
`lower`	the lower bound of the confidence interval of the requested interaction measure.
`upper`	the upper bound of the confidence interval of the requested interaction measure.

References

Chen S-C, Wong R-H, Shiu L-J, Chiou M-C, Lee H (2008). Exposure to mosquito coil smoke may be a risk factor for lung cancer in Taiwan. Journal of Epidemiology 18: 19 - 25.

Hosmer DW, Lemeshow S (1992). Confidence interval estimation of interaction. Epidemiology 3: 452 - 456.

Kalilani L, Atashili J (2006). Measuring additive interaction using odds ratios. Epidemiologic Perspectives & Innovations doi:10.1186/1742-5573-3-5.

Rothman K, Greenland S (1998). Modern Epidemiology. Lippincott - Raven Philadelphia, USA.

Rothman K, Keller AZ (1972). The effect of joint exposure to alcohol and tabacco on risk of cancer of the mouth and pharynx. Journal of Chronic Diseases 23: 711 - 716.

Skrondal A (2003). Interaction as departure from additivity in case-control studies: A cautionary note. American Journal of Epidemiology 158: 251 - 258.

Examples

```
## Data from Rothman and Keller (1972) evaluating the effect of joint exposure
## to alcohol and tabacco on risk of cancer of the mouth and pharynx (cited in
## Hosmer and Lemeshow, 1992):

can <- c(rep(1, times = 231), rep(0, times = 178), rep(1, times = 11),
   rep(0, times = 38))
smk <- c(rep(1, times = 225), rep(0, times = 6), rep(1, times = 166),
```

```
   rep(0, times = 12), rep(1, times = 8), rep(0, times = 3), rep(1, times = 18),
   rep(0, times = 20))
alc <- c(rep(1, times = 409), rep(0, times = 49))
dat <- data.frame(alc, smk, can)

## Table 2 of Hosmer and Lemeshow (1992):
dat.glm01 <- glm(can ~ alc + smk + alc:smk, family = binomial, data = dat)
summary(dat.glm01)

## Rothman defines an alternative coding scheme to be employed for
## parameterising an interaction term. Using this approach, instead of using
## two risk factors and one product term to represent the interaction (as
## above) the risk factors are combined into one variable with (in this case)
## four levels:

## a.neg b.neg: 0 0 0
## a.pos b.neg: 1 0 0
## a.neg b.pos: 0 1 0
## a.pos b.pos: 0 0 1

dat$d <- rep(NA, times = nrow(dat))
dat$d[dat$alc == 0 & dat$smk == 0] <- 0
dat$d[dat$alc == 1 & dat$smk == 0] <- 1
dat$d[dat$alc == 0 & dat$smk == 1] <- 2
dat$d[dat$alc == 1 & dat$smk == 1] <- 3
dat$d <- factor(dat$d)

## Table 3 of Hosmer and Lemeshow (1992):
dat.glm02 <- glm(can ~ d, family = binomial, data = dat)
summary(dat.glm02)

epi.interaction(model = dat.glm02, coeff = c(2,3,4), type = "RERI",
   conf.level = 0.95)
epi.interaction(model = dat.glm02, coeff = c(2,3,4), type = "APAB",
   conf.level = 0.95)
epi.interaction(model = dat.glm02, coeff = c(2,3,4), type = "S",
   conf.level = 0.95)

## Page 455 of Hosmer and Lemeshow (1992):
## RERI: 3.73 (95% CI -1.84 -- 9.32).
## AP[AB]: 0.41 (95% CI -0.07 -- 0.90).
## S: 1.87 (95% CI 0.64 -- 5.41).
```

---

epi.iv *Fixed-effect meta-analysis of binary outcomes using the inverse variance method*

Description

Computes individual study odds or risk ratios for binary outcome data. Computes the summary odds or risk ratio using the inverse variance method. Performs a test of heterogeneity among trials.

Performs a test for the overall difference between groups (that is, after pooling the studies, do treated groups differ significantly from controls?).

Usage

```
epi.iv(ev.trt, n.trt, ev.ctrl, n.ctrl, names, method = "odds.ratio",
   alternative = c("two.sided", "less", "greater"), conf.level = 0.95)
```

Arguments

ev.trt	observed number of events in the treatment group.
n.trt	number in the treatment group.
ev.ctrl	observed number of events in the control group.
n.ctrl	number in the control group.
names	character string identifying each trial.
method	a character string indicating the method to be used. Options are odds.ratio or risk.ratio.
alternative	a character string specifying the alternative hypothesis, must be one of two.sided, greater or less.
conf.level	magnitude of the returned confidence interval. Must be a single number between 0 and 1.

Details

Using this method, the inverse variance weights are used to compute the pooled odds ratios and risk ratios. The inverse variance weights should be used to indicate the weight each trial contributes to the meta-analysis.

alternative = "greater" tests the hypothesis that the inverse variance summary measure of association is greater than 1.

Value

A list containing:

OR	the odds ratio for each trial and the lower and upper bounds of the confidence interval of the odds ratio for each trial.
RR	the risk ratio for each trial and the lower and upper bounds of the confidence interval of the risk ratio for each trial.
OR.summary	the inverse variance summary odds ratio and the lower and upper bounds of the confidence interval of the inverse variance summary odds ratio.
RR.summary	the inverse variance summary risk ratio and the lower and upper bounds of the confidence interval of the inverse variance summary risk ratio.
weights	the raw and inverse variance weights assigned to each trial.
heterogeneity	a vector containing Q the heterogeneity test statistic, df the degrees of freedom and its associated P-value.

Hsq	the relative excess of the heterogeneity test statistic Q over the degrees of freedom df.
Isq	the percentage of total variation in study estimates that is due to heterogeneity rather than chance.
effect	a vector containing z the test statistic for overall treatment effect and its associated P-value.

Note

The inverse variance method performs poorly when data are sparse, both in terms of event rates being low and trials being small. The Mantel-Haenszel method (epi.mh) is more robust when data are sparse.

Using this method, the inverse variance weights are used to compute the pooled odds ratios and risk ratios.

The function checks each strata for cells with zero frequencies. If a zero frequency is found in any cell, 0.5 is added to all cells within the strata.

References

Deeks JJ, Altman DG, Bradburn MJ (2001). Statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. In: Egger M, Davey Smith G, Altman D (eds). Systematic Review in Health Care Meta-Analysis in Context. British Medical Journal, London, 2001, pp. 291 - 299.

Higgins JP, Thompson SG (2002). Quantifying heterogeneity in a meta-analysis. Statistics in Medicine 21: 1539 - 1558.

See Also

epi.dsl, epi.mh, epi.smd

Examples

```
data(epi.epidural)
epi.iv(ev.trt = epi.epidural$ev.trt, n.trt = epi.epidural$n.trt,
   ev.ctrl = epi.epidural$ev.ctrl, n.ctrl = epi.epidural$n.ctrl,
   names = as.character(epi.epidural$trial), method = "odds.ratio",
   alternative = "two.sided", conf.level = 0.95)
```

---

epi.kappa *Kappa statistic*

Description

Computes the kappa statistic and its confidence interval.

Usage

```
epi.kappa(dat, method = "fleiss", alternative = c("two.sided", "less",
   "greater"), conf.level = 0.95)
```

Arguments

dat	an object of class table with the individual cell frequencies.
method	a character string indicating the method to use. Options are fleiss, watson or altman.
alternative	a character string specifying the alternative hypothesis, must be one of two.sided, greater or less.
conf.level	magnitude of the returned confidence interval. Must be a single number between 0 and 1.

Details

Kappa is a measure of agreement beyond the level of agreement expected by chance alone. The observed agreement is the proportion of samples for which both methods (or observers) agree.

The bias and prevalence adjusted kappa (Brt et al. 1993) provides a measure of observed agreement, an index of the bias between observers, and an index of the differences between the overall proportion of 'yes' and 'no' assessments.

Common interpretations for the kappa statistic are as follows: < 0.2 slight agreement, 0.2 - 0.4 fair agreement, 0.4 - 0.6 moderate agreement, 0.6 - 0.8 substantial agreement, > 0.8 almost perfect agreement.

The argument alternative = "greater" tests the hypothesis that kappa is greater than 0.

Value

A list containing the following:

prop.agree	a data frame with obs the observed proportion of agreement and exp the expected proportion of agreement.
pindex	a data frame with the prevalence index, the standard error of the prevalence index and the lower and upper bounds of the confidence interval for the prevalence index.
bindex	a data frame with the bias index, the standard error of the bias index and the lower and upper bounds of the confidence interval for the bias index.
pabak	a data frame with the prevalence and bias corrected kappa statistic and the lower and upper bounds of the confidence interval for the prevalence and bias corrected kappa statistic.
kappa	a data frame with the kappa statistic, the standard error of the kappa statistic and the lower and upper bounds of the confidence interval for the kappa statistic.
z	a data frame containing the z test statistic for kappa and its associated P-value.
mcnemar	a data frame containing the McNemar test statistic for kappa and its associated P-value.

Note

	Obs1 +	Obs1 -	Total
Obs 2 +	a	b	a+b
Obs 2 -	c	d	c+d
Total	a+c	b+d	a+b+c+d=N

The kappa coefficient is influenced by the prevalence of the condition being assessed. A prevalence effect exists when the proportion of agreements on the positive classification differs from that of the negative classification. If the prevalence index is high (that is, the prevalence of a positive rating is very high or very low) chance agreement is also high and the value of kappa is reduced accordingly. The effect of prevalence on kappa is greater for large values of kappa than for small values (Byrt et al. 1993). Using the notation above, the prevalence index is calculated as `((a/N) - (d/N))`. Confidence intervals for the prevalence index are based on methods used for a difference in two proportions. See Rothman (2002, p 135 equation 7-2) for details.

Bias is the extent to which raters disagree on the proportion of positive (or negative) cases. Bias affects interpretation of the kappa coefficient. When there is a large amount of bias, kappa is higher than when bias is low or absent. In contrast to prevalence, the effect of bias is greater when kappa is small than when it is large (Byrt et al. 1993). Using the notation above, the bias index is calculated as `((a + b)/N - (a + c)/N)`. Confidence intervals for the bias index are based on methods used for a difference in two proportions. See Rothman (2002, p 135 equation 7-2) for details.

The McNemar test is used to test for the presence of bias. A statistically significant McNemar test (generally if $P < 0.05$) shows that there is evidence of a systematic difference between the proportion of 'positive' responses from the two methods. If one method provides the 'true values' (i.e. it is regarded as the gold standard method) the absence of a systematic difference implies that there is no bias. However, a non-significant result indicates only that there is no evidence of a systematic effect. A systematic effect may be present, but the power of the test may be inadequate to determine its presence.

References

Altman DG, Machin D, Bryant TN, Gardner MJ (2000). Statistics with Confidence, second edition. British Medical Journal, London, pp. 116 - 118.

Byrt T, Bishop J, Carlin JB (1993). Bias, prevalence and kappa. Journal of Clinical Epidemiology 46: 423 - 429.

Dohoo I, Martin W, Stryhn H (2010). Veterinary Epidemiologic Research, second edition. AVC Inc, Charlottetown, Prince Edward Island, Canada, pp. 98 - 99.

Fleiss JL, Levin B, Paik MC (2003). Statistical Methods for Rates and Proportions, third edition. John Wiley & Sons, London, 598 - 626.

Rothman KJ (2002). Epidemiology An Introduction. Oxford University Press, London, pp. 130 - 143.

Silva E, Sterry RA, Kolb D, Mathialagan N, McGrath MF, Ballam JM, Fricke PM (2007) Accuracy of a pregnancy-associated glycoprotein ELISA to determine pregnancy status of lactating dairy cows twenty-seven days after timed artificial insemination. Journal of Dairy Science 90: 4612 - 4622.

Sim J, Wright CC (2005) The kappa statistic in reliability studies: Use, interpretation, and sample size requirements. Physical Therapy 85: 257 - 268.

Watson PF, Petrie A (2010) Method agreement analysis: A review of correct methodology. Theriogenology 73: 1167 - 1179.

Examples

```
## EXAMPLE 1:
## Kidney samples from 291 salmon were split with one half of the
## samples sent to each of two laboratories where an IFAT test
## was run on each sample. The following results were obtained:

## Lab 1 positive, lab 2 positive: 19
## Lab 1 positive, lab 2 negative: 10
## Lab 1 negative, lab 2 positive: 6
## Lab 1 negative, lab 2 negative: 256

dat <- as.table(matrix(c(19,10,6,256), nrow = 2, byrow = TRUE))
colnames(dat) <- c("L1-pos","L1-neg")
rownames(dat) <- c("L2-pos","L2-neg")

epi.kappa(dat, method = "fleiss", alternative = "greater", conf.level = 0.95)

## The z test statistic is 11.53 (P < 0.01). We accept the alternative
## hypothesis that the kappa statistic is greater than zero.

## The proportion of agreements after chance has been excluded is
## 0.67 (95% CI 0.56 to 0.79). We conclude that, on the basis of
## this sample, that there is substantial agreement between the two
## laboratories.

## EXAMPLE 2 (from Watson and Petrie 2010, page 1170):
## Silva et al. (2007) compared an early pregnancy enzyme-linked immunosorbent
## assay test for pregnancy associated glycoprotein on blood samples collected
## from lactating dairy cows at day 27 after artificial insemination with
## transrectal ultrasound (US) diagnosis of pregnancy at the same stage.
## The results were as follows:

## ELISA positive, US positive: 596
## ELISA positive, US negative: 61
## ELISA negative, US positive: 29
## ELISA negative, Ul negative: 987

dat <- as.table(matrix(c(596,61,29,987), nrow = 2, byrow = TRUE))
colnames(dat) <- c("US-pos","US-neg")
rownames(dat) <- c("ELISA-pos","ELISA-neg")

epi.kappa(dat, method = "watson", alternative = "greater", conf.level = 0.95)
```

```
## The proportion of agreements after chance has been excluded is
## 0.89 (95% CI 0.86 to 0.91). We conclude that that there is substantial
## agreement between the two pregnancy diagnostic methods.
```

`epi.ltd` *Lactation to date and standard lactation milk yields*

Description

Calculate lactation to date and standard lactation (that is, 305 or 270 day) milk yields.

Usage

```
epi.ltd(dat, std = "305")
```

Arguments

`dat`	an eight column data frame listing (in order) cow identifier, herd test identifier, lactation number, herd test days in milk, lactation length (`NA` if lactation incomplete), herd test milk yield (litres), herd test fat (percent), and herd test protein (percent).
`std`	`std = "305"` returns 305-day milk volume, fat, and protein yield. `std = "270"` returns 270-day milk volume, fat, and protein yield.

Details

Lactation to date yields will only be calculated if there are four or more herd test events.

Value

A data frame with nine elements: `ckey` cow identifier, `lact` lactation number, `llen` lactation length, `vltd` milk volume (litres) to last herd test or dry off date (computed on the basis of lactation length, `fltd` fat yield (kilograms) to last herd test or dry off date (computed on the basis of lactation length, `pltd` protein yield (kilograms) to last herd test or dry off date (computed on the basis of lactation length, `vstd` 305-day or 270-day milk volume yield (litres), `fstd` 305-day or 270-day milk fat yield (kilograms), and `pstd` 305-day or 270-day milk protein yield (kilograms).

Author(s)

Nicolas Lopez-Villalobos (IVABS, Massey University, Palmerston North New Zealand) and Mark Stevenson (Faculty of Veterinary and Agricultural Sciences, The University of Melbourne, Australia).

References

Kirkpatrick M, Lofsvold D, Bulmer M (1990). Analysis of the inheritance, selection and evolution of growth trajectories. Genetics 124: 979 - 993.

Examples

```
## Generate some herd test data:
ckey <- rep(1, times = 12)
pkey <- 1:12
lact <- rep(1:2, each = 6)
dim <- c(25, 68, 105, 145, 200, 240, 30, 65, 90, 130, 190, 220)
llen <- c(280, 280, 280, 280, 280, 280, NA, NA, NA, NA, NA, NA)
vol <- c(18, 30, 25, 22, 18, 12, 20, 32, 27, 24, 20, 14)
fat <- c(4.8, 4.3, 4.5, 4.7, 4.8, 4.9, 4.8, 4.3, 4.5, 4.7, 4.8, 4.9)/100
pro <- c(3.7, 3.5, 3.6, 3.7, 3.8, 3.9, 3.7, 3.5, 3.6, 3.7, 3.8, 3.9)/100
dat <- data.frame(ckey, pkey, lact, dim, llen, vol, fat, pro)

## Lactation to date and 305-day milk, fat, and protein yield:
epi.ltd(dat, std = "305")

## Lactation to date and 270-day milk, fat, and protein yield:
epi.ltd(dat, std = "270")
```

---

epi.meansize *Sample size, power and minimum detectable difference when comparing means*

Description

Calculates the sample size, power or minimum detectable difference when comparing means.

Usage

```
epi.meansize(treat, control, n, sigma, power, r = 1, design = 1,
   sided.test = 2, conf.level = 0.95)
```

Arguments

treat	the expected value for the treatment group (see below).
control	the expected value for the control group (see below).
n	scalar, defining the total number of subjects in the study (i.e. the number in the treatment and control group).
sigma	the expected standard deviation of the variable of interest for both treatment and control groups.
power	scalar, the required study power.
r	scalar, the number in the treatment group divided by the number in the control group.
design	scalar, the estimated design effect.

sided.test	use a one- or two-sided test? Use a two-sided test if you wish to evaluate whether or not the treatment group is better or worse than the control group. Use a one-sided test to evaluate whether or not the treatment group is better than the control group.
conf.level	scalar, defining the level of confidence in the computed result.

Details

The methodology in this function follows the approach described in Chapter 8 of Woodward (2005), pp. 381 - 426.

Value

A list containing the following:

n.total	the total number of subjects required for the specified level of confidence and power, respecting the requirement for r times as many individuals in the treatment group compared with the control group.
n.treat	the total number of subjects in the treatment group for the specified level of confidence and power, respecting the requirement for r times as many individuals in the treatment group compared with the control group.
n.control	the total number of subjects in the control group for the specified level of confidence and power, respecting the requirement for r times as many individuals in the treatment group compared with the control group.
power	the power of the study given the number of study subjects, the expected effect size and level of confidence.
delta	the minimum detectable difference given the specified level of confidence and power.

Note

The power of a study is its ability to demonstrate the presence of an association, given that an association actually exists.

A detailed description of sample size calculations for case-control studies (with numerous worked examples, many of them reproduced below) is provided by Woodward (2005), pages 381 to 426.

See the documentation for epi.cohortsize which provides an example using the design facility implemented in this function.

References

Kelsey JL, Thompson WD, Evans AS (1986). Methods in Observational Epidemiology. Oxford University Press, London, pp. 254 - 284.

Woodward M (2005). Epidemiology Study Design and Data Analysis. Chapman & Hall/CRC, New York, pp. 381 - 426.

Examples

```
## EXAMPLE 1 (from Woodward 2005 p. 399):
## Supposed we wish to test, at the 5% level of significance, the hypothesis
## that cholesterol means in a population are equal in two study years against
## the one-sided alternative that the mean is higher in the second of the
## two years. Suppose that equal sized samples will be taken in each year,
## but that these will not necessarily be from the same individuals (i.e. the
## two samples are drawn independently). Our test is to have a power of 0.95
## at detecting a difference of 0.5 mmol/L. The standard deviation of serum
## cholesterol in humans is assumed to be 1.4 mmol/L.

epi.meansize(treat = 5, control = 4.5, n = NA, sigma = 1.4, power = 0.95,
   r = 1, design = 1, sided.test = 1, conf.level = 0.95)

## To satisfy the study requirements 340 individuals need to be tested: 170 in
## the first year and 170 in the second year.


## EXAMPLE 2 (from Woodward 2005 pp. 399 - 400):
## Women taking oral contraceptives sometimes experience anaemia due to
## impaired iron absorption. A study is planned to compare the use of iron
## tablets against a course of placebos. Oral contraceptive users are
## randomly allocated to one of the two treatment groups and mean serum
## iron concentration compared after 6 months. Data from previous studies
## indicates that the standard deviation of the increase in iron
## concentration will be around 4 micrograms% over a 6-month period.
## The average increase in serum iron concentration without supplements is
## also thought to be 4 micrograms%. The investigators wish to be 90% sure
## of detecting when the supplement doubles the serum iron concentration using
## a two-sided 5% significance test. It is decided to allocate 4 times as many
## women to the treatment group so as to obtain a better idea of its effect.
## How many women should be enrolled in this study?

epi.meansize(treat = 8, control = 4, n = NA, sigma = 4, power = 0.90,
   r = 4, design = 1, sided.test = 2, conf.level = 0.95)

## The estimated sample size is 70. We allocate 70/5 = 14 women to the
## placebo group and four times as many (56) to the iron treatment group.
```

`epi.mh` *Fixed-effects meta-analysis of binary outcomes using the Mantel-Haenszel method*

Description

Computes individual study odds or risk ratios for binary outcome data. Computes the summary odds or risk ratio using the Mantel-Haenszel method. Performs a test of heterogeneity among trials. Performs a test for the overall difference between groups (that is, after pooling the studies, do treated groups differ significantly from controls?).

Usage

```
epi.mh(ev.trt, n.trt, ev.ctrl, n.ctrl, names, method = "odds.ratio",
   alternative = c("two.sided", "less", "greater"), conf.level = 0.95)
```

Arguments

ev.trt	observed number of events in the treatment group.
n.trt	number in the treatment group.
ev.ctrl	observed number of events in the control group.
n.ctrl	number in the control group.
names	character string identifying each trial.
method	a character string indicating the method to be used. Options are odds.ratio or risk.ratio.
alternative	a character string specifying the alternative hypothesis, must be one of two.sided, greater or less.
conf.level	magnitude of the returned confidence interval. Must be a single number between 0 and 1.

Details

alternative = "greater" tests the hypothesis that the Mantel-Haenszel summary measure of association is greater than 1.

Value

A list containing the following:

OR	the odds ratio for each trial and the lower and upper bounds of the confidence interval of the odds ratio for each trial.
RR	the risk ratio for each trial and the lower and upper bounds of the confidence interval of the risk ratio for each trial.
OR.summary	the Mantel-Haenszel summary odds ratio and the lower and upper bounds of the confidence interval of the Mantel-Haenszel summary odds ratio.
RR.summary	the Mantel-Haenszel summary risk ratio and the lower and upper bounds of the confidence interval of the Mantel-Haenszel summary risk ratio.
weights	the raw and inverse variance weights assigned to each trial.
heterogeneity	a vector containing Q the heterogeneity test statistic, df the degrees of freedom and its associated P-value.
Hsq	the relative excess of the heterogeneity test statistic Q over the degrees of freedom df.
Isq	the percentage of total variation in study estimates that is due to heterogeneity rather than chance.
effect	a vector containing z the test statistic for overall treatment effect and its associated P-value.

Note

Using this method, the pooled odds and risk ratios are computed using the raw individual study weights. The methodology for computing the Mantel-Haenszel summary odds ratio follows the approach decribed in Deeks, Altman and Bradburn MJ (2001, pp 291 - 299).

The function checks each strata for cells with zero frequencies. If a zero frequency is found in any cell, 0.5 is added to all cells within the strata.

References

Deeks JJ, Altman DG, Bradburn MJ (2001). Statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. In: Egger M, Davey Smith G, Altman D (eds). Systematic Review in Health Care Meta-Analysis in Context. British Medical Journal, London, 2001, pp. 291 - 299.

Higgins JP, Thompson SG (2002). Quantifying heterogeneity in a meta-analysis. Statistics in Medicine 21: 1539 - 1558.

See Also

epi.dsl, epi.iv, epi.smd

Examples

```
data(epi.epidural)
epi.mh(ev.trt = epi.epidural$ev.trt, n.trt = epi.epidural$n.trt,
   ev.ctrl = epi.epidural$ev.ctrl, n.ctrl = epi.epidural$n.ctrl,
   names = as.character(epi.epidural$trial), method = "odds.ratio",
   alternative = "two.sided", conf.level = 0.95)
```

---

epi.nomogram *Post-test probability of disease given sensitivity and specificity of a test*

Description

Computes the post-test probability of disease given sensitivity and specificity of a test.

Usage

```
epi.nomogram(se, sp, lr, pre.pos, verbose = FALSE)
```

Arguments

se	test sensitivity (0 - 1).
sp	test specificity (0 - 1).
lr	a vector of length 2 listing the positive and negative likelihood ratio (respectively) of the test. Ignored if se and sp are not null.
pre.pos	the pre-test probability of the outcome.
verbose	logical, indicating whether detailed or summary results are to be returned.

Value

A list containing the following:

lr	the likelihood ratio of a positive and negative test.
prob	the post-test probability of the outcome given a positive and negative test.

References

Caraguel C, Vanderstichel R (2013). The two-step Fagan's nomogram: ad hoc interpretation of a diagnostic test result without calculation. Evidence Based Medicine 18: 125 - 128.

Hunink M, Glasziou P (2001). Decision Making in Health and Medicine - Integrating Evidence and Values. Cambridge University Press, pp. 128 - 156.

Examples

```
## EXAMPLE 1:
## You are presented with a dog with lethargy, exercise intolerance,
## weight gain and bilaterally symmetric truncal alopecia. You are
## suspicious of hypothyroidism and take a blood sample to measure
## basal serum thyroxine (T4).

## You believe that around 5% of dogs presented to your clinic with
## a signalment of general debility have hypothyroidism. The serum T4
## has a sensitivity of 0.89 and specificity of 0.85 for diagnosing
## hypothyroidism in the dog. The laboratory reports a serum T4
## concentration of 22.0 nmol/L (reference range 19.0 to 58.0 nmol/L).
## What is the post-test probability that this dog is hypothyroid?

epi.nomogram(se = 0.89, sp = 0.85, lr = NA, pre.pos = 0.05, verbose = FALSE)

## Given a positive test result, the post-test probability of being
## disease positive is 0.24.

## Given a negative test result, the post-test probability of being
## disease negative is 0.0068.

## EXAMPLE 2:
## A dog is presented to you with severe pruritis. You suspect sarcoptic
## mange and decide to take a skin scraping (LR+ 9000; LR- 0.1). The scrape
## returns a negative result (no mites are seen). What is the post-test
## probability that your patient has sarcoptic mange? You recall that you
## diagnose around 3 cases of sarcoptic mange per year in a clinic that
## sees approximately 2 -- 3 dogs per week presented with pruritic skin disease.

pre.pos <- 3 / (3 * 52)
epi.nomogram(se = NA, sp = NA, lr = c(9000, 0.1), pre.pos = pre.pos,
   verbose = FALSE)

## If the skin scraping is negative the post-test probability that this dog
## has sarcoptic mange is 0.002.
```

epi.noninfb *Estimate the sample size for a parallel non-inferiority trial, binary outcomes*

Description

Computes the sample size for a parallel non-inferiority trial with a binary outcome variable.

Usage

```
epi.noninfb(treat, control, delta, n, r = 1, power, alpha)
```

Arguments

treat	the expected proportion of successes in the treatment group.
control	the expected proportion of successes in the control group.
delta	the equivalence limit, expressed as a proportion.
n	scalar, the total number of study subjects in the trial.
r	scalar, the number in the treatment group divided by the number in the control group.
power	scalar, the required study power.
alpha	scalar, defining the desired alpha level.

Value

A list containing one or more of the following:

n.treat	the required number of study subject in the treatment group.
n.control	the required number of study subject in the control group.
n.total	the total number of study subjects required.

Note

Consider a clinical trial comparing two groups, a standard treatment (s) and a new treatment (n). In each group, a proportion of subjects respond to the treatment: Ps and Pn.

With a superiority trial we specify the maximum acceptable difference between Pn and Ps as delta. The null hypothesis is H0: Pn - Ps <= delta and the alternative hypothesis is H1: Pn - Ps > delta.

An equivalence trial is used if want to prove that two treatments produce the same clinical outcomes. With an equivalence trial, we specify the maximum acceptable difference between Pn and Ps as delta. The null hypothesis is H0: |Ps - Pn| >= delta and the alternative hypothesis is H1: |Ps - Pn| < delta. In bioequivalence trials, a 90% confidence interval is often used. The value of the maximum acceptable difference delta is chosen so that a patient will not detect any change in effect when replacing the standard treatment with the new treatment.

With a non-inferiority trial, we specify the maximum acceptable difference between Pn and Ps as delta. The null hypothesis is H0: Ps - Pn >= delta and the alternative hypothesis is H1: Ps - Pn

< delta. The aim of a non-inferiority trial is show that a new treatment is not (much) inferior to a standard treatment. Showing non-inferiority can be of interest because: (a) it is often not ethically possible to do a placebo-controlled trial, (b) the new treatment is not expected to be better than the standard treatment on primary efficacy endpoints, but is safer, (c) the new treatment is not expected to be better than the standard treatment on primary efficacy endpoints, but is cheaper to produce or easier to administer, (d) the new treatment is not expected to be better than the standard treatment on primary efficacy endpoints in clinical trial, but compliance will be better outside the clinical trial and hence efficacy better outside the trial.

For a summary of the key features of superiority, equivalence and non-inferiority trials, refer to the documentation for epi.equivb.

When calculating the power of a study, note that the variable n refers to the total study size (that is, the number of subjects in the treatment group plus the number in the control group).

References

Blackwelder WC (1982). Proving the null hypothesis in clinical trials. Controlled Clinical Trials 3: 345 - 353.

Ewald B (2013). Making sense of equivalence and non-inferiority trials. Australian Prescriber 36: 170 - 173.

Julious SA (2004). Sample sizes for clinical trials with normal data. Statistics in Medicine 23: 1921 - 1986.

Julious SA (2009). Estimating Samples Sizes in Clinical Trials. CRC, New York.

Machin D, Campbell MJ, Tan SB, Tan SH (2009). Sample Size Tables for Clinical Studies. Wiley Blackwell, New York.

Scott IA (2009). Non-inferiority trials: determining whether alternative treatments are good enough. Medical Journal of Australia 190: 326 - 330.

Zhong B (2009). How to calculate sample size in randomized controlled trial? Journal of Thoracic Disease 1: 51 - 54.

Examples

```
## EXAMPLE 1:
## Suppose it is of interest to establish non-inferiority of a new treatment
## as compared to the currently used standard treatment. A difference of less
## than 10% is of no clinical importance. Thus, the non-inferiority margin
## (delta) is set at 0.10. Assume the true cure rate for the new treatment
## is 0.85 and the control is 0.65. Assuming a one-sided test size of 2.5% and
## a power of 90% how many subjects should be included in the trial?

epi.noninfb(treat = 0.85, control = 0.65, delta = 0.10, n = NA, r = 1,
   power = 0.80, alpha = 0.025)

## A total of 558 subjects need to be enrolled in the trial, 279 in the
## treatment group and 279 in the control group.

## EXAMPLE 1 (cont.):
## Suppose only 400 subjects were enrolled in the trial, 200 in the treatment
## group and 200 in the control group. What is the estimated study power?
```

```
epi.noninfb(treat = 0.85, control = 0.65, delta = 0.10, n = 400, r = 1,
   power = NA, alpha = 0.025)

## With only 500 subjects the estimated study power is 0.66.
```

`epi.noninfc` *Estimate the sample size for a parallel equivalence trial, continuous outcomes*

Description

Computes the sample size for a parallel equivalence trial with a continuous outcome variable.

Usage

```
epi.noninfc(treat, control, sd, delta, n, r = 1, power, alpha)
```

Arguments

`treat`	the expected mean of the outcome of interest in the treatment group.
`control`	the expected mean of the outcome of interest in the control group.
`sd`	the expected population standard deviation of the outcome of interest.
`delta`	the equivalence limit, expressed as a proportion.
`n`	scalar, the total number of study subjects in the trial.
`r`	scalar, the number in the treatment group divided by the number in the control group.
`power`	scalar, the required study power.
`alpha`	scalar, defining the desired alpha level.

Value

A list containing one or more of the following:

`n.treat`	the required number of study subject in the treatment group.
`n.control`	the required number of study subject in the control group.
`n.total`	the total number of study subjects required.

Note

Consider a clinical trial comparing two groups, a standard treatment (s) and a new treatment (n). In each group, a proportion of subjects respond to the treatment: Ps and Pn.

With a superiority trial we specify the maximum acceptable difference between Pn and Ps as `delta`. The null hypothesis is H0: Pn - Ps <= `delta` and the alternative hypothesis is H1: Pn - Ps > `delta`.

An equivalence trial is used if want to prove that two treatments produce the same clinical outcomes. With an equivalence trial, we specify the maximum acceptable difference between Pn and Ps as `delta`. The null hypothesis is H0: |Ps - Pn| >= `delta` and the alternative hypothesis is H1: |Ps - Pn| < `delta`. In bioequivalence trials, a 90% confidence interval is often used. The value of the maximum acceptable difference `delta` is chosen so that a patient will not detect any change in effect when replacing the standard treatment with the new treatment.

With a non-inferiority trial, we specify the maximum acceptable difference between Pn and Ps as `delta`. The null hypothesis is H0: Ps - Pn >= `delta` and the alternative hypothesis is H1: Ps - Pn < `delta`. The aim of a non-inferiority trial is show that a new treatment is not (much) inferior to a standard treatment. Showing non-inferiority can be of interest because: (a) it is often not ethically possible to do a placebo-controlled trial, (b) the new treatment is not expected to be better than the standard treatment on primary efficacy endpoints, but is safer, (c) the new treatment is not expected to be better than the standard treatment on primary efficacy endpoints, but is cheaper to produce or easier to administer, (d) the new treatment is not expected to be better than the standard treatment on primary efficacy endpoints in clinical trial, but compliance will be better outside the clinical trial and hence efficacy better outside the trial.

For a summary of the key features of superiority, equivalence and non-inferiority trials, refer to the documentation for `epi.equivb`.

When calculating the power of a study, note that the variable `n` refers to the total study size (that is, the number of subjects in the treatment group plus the number in the control group).

References

Blackwelder WC (1982). Proving the null hypothesis in clinical trials. Controlled Clinical Trials 3: 345 - 353.

Ewald B (2013). Making sense of equivalence and non-inferiority trials. Australian Prescriber 36: 170 - 173.

Julious SA (2004). Sample sizes for clinical trials with normal data. Statistics in Medicine 23: 1921 - 1986.

Julious SA (2009). Estimating Samples Sizes in Clinical Trials. CRC, New York.

Machin D, Campbell MJ, Tan SB, Tan SH (2009). Sample Size Tables for Clinical Studies. Wiley Blackwell, New York.

Scott IA (2009). Non-inferiority trials: determining whether alternative treatments are good enough. Medical Journal of Australia 190: 326 - 330.

Zhong B (2009). How to calculate sample size in randomized controlled trial? Journal of Thoracic Disease 1: 51 - 54.

Examples

```
## EXAMPLE 1 (from Chow S, Shao J, Wang H 2008, p. 64):
```

```
## A pharmaceutical company is interested in conducting a clinical trial
## to compare two cholesterol lowering agents for treatment of patients with
## congestive hear disease using a parallel design. The primary efficacy
## parameter is the LDL. In what follows, we will consider the situation
## where the intended trial is for testing non-inferiority of mean responses
## in LDL. Assume that 80% power is required at a 5% level of significance.

## In this example, we assume a 5% (i.e. delta = 0.05) change of LDL is
## considered of clinically meaningful difference. Assume the standard
## of LDL is 0.10 and the LDL concentration in the treatment group is 0.20
## units and the LDL concentration in the control group is 0.20 units.

epi.noninfc(treat = 0.20, control = 0.20, sd = 0.10, delta = 0.05, n = NA,
   r = 1, power = 0.80, alpha = 0.05)

## A total of 100 subjects need to be enrolled in the trial, 50 in the
## treatment group and 50 in the control group.
```

`epi.occc` *Overall concordance correlation coefficient (OCCC)*

Description

Overall concordance correlation coefficient (OCCC) for agreement on a continuous measure based on Lin (1989, 2000) and Barnhart et al. (2002).

Usage

```
epi.occc(dat, na.rm = FALSE, pairs = FALSE)

## S3 method for class 'epi.occc'
print(x, ...)

## S3 method for class 'epi.occc'
summary(object, ...)
```

Arguments

`dat`	a matrix, or a matrix like object. Rows correspond to cases/observations, columns corresponds to raters/variables.
`na.rm`	logical. Should missing values (including `NaN`) be removed?
`pairs`	logical. Should the return object contain pairwise statistics? See Details.
`x, object`	an object of class `epi.occc`.
`...`	further arguments passed to `print` methods.

Details

The index proposed by Barnhart et al. (2002) is the same as the index suggested by Lin (1989) in the section of future studies with a correction of a typographical error in Lin (2000).

Value

An object of class `epi.occc` with the following list elements (notation follows Barnhart et al. 2002):

- `occc`: the value of the overall concordance correlation coefficient (ρ_o^c),
- `oprec`: overall precision (ρ),
- `oaccu`: overall accuracy (χ^a),
- `pairs`: a list with following elements (only if `pairs = TRUE`, otherwise `NULL`; column indices for the pairs (j,k) follow lower-triangle column-major rule based on a `ncol(x)` times `ncol(x)` matrix),
  - `ccc`: pairwise CCC values (ρ_{jk}^c),
  - `prec`: pairwise precision values (ρ_{jk}),
  - `accu`: pairwise accuracy values (χ_{jk}^a),
  - `ksi`: pairwise weights (ξ_{jk}),
  - `scale`: pairwise scale values (v_{jk}),
  - `location`: pairwise location values (u_{jk}),
- `data.name`: name of the input data `dat`.

Author(s)

Peter Solymos, solymos@ualberta.ca.

References

Barnhart H X, Haber M, Song J (2002). Overall concordance correlation coefficient for evaluating agreement among multiple observers. Biometrics 58: 1020 - 1027.

Lin L (1989). A concordance correlation coefficient to evaluate reproducibility. Biometrics 45: 255 - 268.

Lin L (2000). A note on the concordance correlation coefficient. Biometrics 56: 324 - 325.

See Also

`epi.ccc`

Examples

```
## Generate some artificial ratings data:
set.seed(1234)
p <- runif(10, 0, 1)
x <- replicate(n = 5, expr = rbinom(10, 4, p) + 1)

rval <- epi.occc(dat = x, pairs = TRUE)
print(rval); summary(rval)
```

`epi.offset` *Create offset vector*

Description

Creates an offset vector based on a list.

Usage

```
epi.offset(id.names)
```

Arguments

`id.names`	a list identifying the [location] of each case. This must be a factor.

Details

This function is useful for supplying spatial data to WinBUGS.

Value

A vector of length (1 + length of `id`). The first element of the offset vector is 1, corresponding to the position at which data for the first factor appears in id. The second element of the offset vector corresponds to the position at which the second factor appears in `id` and so on. The last element of the offset vector corresponds to the length of the `id` list.

References

Bailey TC, Gatrell AC (1995). Interactive Spatial Data Analysis. Longman Scientific & Technical. London.

Langford IH (1994). Using empirical Bayes estimates in the geographical analysis of disease risk. Area 26: 142 - 149.

Examples

```
dat <- c(1,1,1,2,2,2,2,3,3,3)
dat <- as.factor(dat)

offset <- epi.offset(dat)
offset
## [1] 1 4 8 10
```

epi.pooled *Estimate herd test characteristics when pooled sampling is used*

Description

We may wish to designate a group of individuals (e.g. a herd) as being either diseased or non-diseased on the basis of pooled samples. This function estimates sensitivity and specificity of this testing regime at the group (or herd) level.

Usage

```
epi.pooled(se, sp, P, m, r)
```

Arguments

se	a vector of length one defining the sensitivity of the individual test used.
sp	a vector of length one defining the specificity of the individual test used.
P	scalar, defining the estimated true prevalence.
m	scalar, defining the number of individual samples to make up a pooled sample.
r	scalar, defining the number of pooled samples per group (or herd).

Value

A list containing the following:

HAPneg	the apparent prevalence in a disease negative herd.
HSe	the estimated group (herd) level sensitivity.
HSp	the estimated group (herd) level specificity.

References

Dohoo I, Martin W, Stryhn H (2003). Veterinary Epidemiologic Research. AVC Inc, Charlottetown, Prince Edward Island, Canada, pp. 115 - 117 .

Christensen J, Gardner IA (2000). Herd-level interpretation of test results for epidemiologic studies of animal diseases. Preventive Veterinary Medicine 45: 83 - 106.

Examples

```
## We want to test dairy herds for Johne's disease using faecal culture
## which has a sensitivity and specificity of 0.647 and 0.981, respectively.
## Suppose we pool faecal samples from five cows together and use six pooled
## samples per herd. What is the herd level sensitivity and specificity
## based on this approach (assuming homogenous mixing)?

epi.pooled(se = 0.647, sp = 0.981, P = 0.12, m = 5 , r = 6)
```

```
## Herd level sensitivity is 0.927, herd level specificity is 0.562.
## Sensitivity at the herd level is increased using the pooled sampling
## approach; herd level specificity is decreased.
```

`epi.popsize` *Estimate population size*

Description

Estimates population size on the basis of capture-recapture sampling.

Usage

```
epi.popsize(T1, T2, T12, conf.level = 0.95, verbose = FALSE)
```

Arguments

`T1`	an integer representing the number of individuals tested in the first round.
`T2`	an integer representing the number of individuals tested in the second round.
`T12`	an integer representing the number of individuals tested in both the first and second round.
`conf.level`	magnitude of the returned confidence interval. Must be a single number between 0 and 1.
`verbose`	logical indicating whether detailed or summary results are to be returned.

Value

Returns the estimated population size and an estimate of the numbers of individuals that remain untested.

References

Cannon RM, Roe RT (1982). Livestock Disease Surveys A Field Manual for Veterinarians. Australian Government Publishing Service, Canberra, pp. 34.

Examples

```
## In a field survey 400 feral pigs are captured, marked and then released.
## On a second occassion 40 of the orignal capture are found when another 400
## pigs are captured. Estimate the size of this feral pig population. Estimate
## the number of feral pigs that have not been tested.

epi.popsize(T1 = 400, T2 = 400, T12 = 40, conf.level = 0.95, verbose = FALSE)

## Estimated population size: 4000 (95% CI 3125 - 5557)
## Estimated number of untested pigs: 3240 (95% CI 2365 - 4797)
```

epi.prcc *Partial rank correlation coefficients*

Description

Compute partial rank correlation coefficients.

Usage

```
epi.prcc(dat, sided.test = 2)
```

Arguments

dat	a data frame comprised of K + 1 columns and N rows, where K represents the number of model parameters being evaluated and N represents the number of replications of the model. The last column of the data frame (i.e. column K + 1) provides the model output.
sided.test	use a one- or two-sided test? Use a two-sided test if you wish to evaluate whether or not the partial rank correlation coefficient is greater than or less than zero. Use a one-sided test to evaluate whether or not the partial rank correlation coefficient is greater than zero.

Details

If the number of parameters K is greater than the number of model replications N an error will be returned.

Value

A data frame with three elements: gamma the partial rank corellation coefficient between each input parameter and the outcome, test.statistic the test statistic used to determine the significance of non-zero values of gamma, and p.value the associated P-value.

Author(s)

Jonathon Marshall, J.C.Marshall@massey.ac.nz.

References

Blower S, Dowlatabladi H (1994). Sensitivity and uncertainty analysis of complex models of disease transmission: an HIV model, as an example. International Statistical Review 62: 229 - 243.

Sanchez M, Blower S (1997) Uncertainty and sensitivity analysis of the basic reproductive rate. American Journal of Epidemiology 145: 1127 - 1137.

Examples

```
## Create a matrix of simulation results:
x1 <- data.frame(rnorm(n = 10, mean = 120, sd = 10))
x2 <- data.frame(rnorm(n = 10, mean = 80, sd = 5))
x3 <- data.frame(rnorm(n = 10, mean = 40, sd = 20))
y <- 2 + (0.5 * x1) + (0.7 * x2) + (0.2 * x3)

dat <- data.frame(cbind(X1 = x1, X2 = x2, X3 = x3, Y = y))
epi.prcc(dat, sided.test = 2)
```

---

epi.prev *Estimate true prevalence*

Description

Computes the true prevalence of a disease in a population on the basis of an imperfect test.

Usage

```
epi.prev(pos, tested, se, sp, method = "wilson", units = 100, conf.level = 0.95)
```

Arguments

pos	a vector listing the count of positive test results for each population.
tested	a vector listing the count of subjects tested for each population.
se	test sensitivity (0 - 1). se can either be a single number or a vector of the same length as pos. See the examples, below, for details.
sp	test specificity (0 - 1). sp can either be a single number or a vector of the same length as pos. See the examples, below, for details.
method	a character string indicating the confidence interval calculation method to use. Options are "c-p" (Cloppper-Pearson), "sterne" (Sterne), "blaker" (Blaker) and "wilson" (Wilson).
units	multiplier for the prevalence estimates.
conf.level	magnitude of the returned confidence interval. Must be a single number between 0 and 1.

Details

Appropriate confidence intervals for the adjusted prevalence estimate are provided, accounting for the change in variance that arises from imperfect test sensitivity and specificity (see Reiczigel et al 2010 for details).

The Clopper-Pearson method is known to be too conservative for two-sided intervals (Blaker 2000, Agresti and Coull 1998). Blaker's and Sterne's methods (Blaker 2000, Sterne 1954) provide smaller exact two-sided confidence interval estimates.

Value

A list containing the following:

ap	the point estimate of apparent prevalence and the lower and upper bounds of the confidence interval around the apparent prevalence estimate.
tp	the point estimate of the true prevalence and the lower and upper bounds of the confidence interval around the true prevalence estimate.

Note

This function uses apparent prevalence, test sensitivity and test specificity to estimate true prevalence (after Rogan and Gladen, 1978). Confidence intervals for the apparent and true prevalence estimates are based on code provided by Reiczigel et al. (2010).

References

Abel U (1993). DieBewertung Diagnostischer Tests. Hippokrates, Stuttgart.

Agresti A, Coull BA (1998). Approximate is better than 'exact' for interval estimation of binomial proportions. American Statistician 52: 119 - 126.

Blaker H (2000). Confidence curves and improved exact confidence intervals for discrete distributions. Canadian Journal of Statistics 28: 783 - 798.

Clopper CJ, Pearson ES (1934). The use of confidence of fiducial limits illustrated in the case of the binomial. Biometrika 26: 404 - 413.

Gardener IA, Greiner M (1999). Advanced Methods for Test Validation and Interpretation in Veterinary Medicince. Freie Universitat Berlin, ISBN 3-929619-22-9; 80 pp.

Messam L, Branscum A, Collins M, Gardner I (2008) Frequentist and Bayesian approaches to prevalence estimation using examples from Johne's disease. Animal Health Research Reviews 9: 1 - 23.

Reiczigel J, Foldi J, Ozsvari L (2010). Exact confidence limits for prevalence of disease with an imperfect diagnostic test. Epidemiology and Infection 138: 1674 - 1678.

Rogan W, Gladen B (1978). Estimating prevalence from results of a screening test. American Journal of Epidemiology 107: 71 - 76.

Sterne TE (1954). Some remarks on confidence or fiducial limits. Biometrika 41: 275 - 278.

Examples

```
## A simple random sample of 150 cows from a herd of 2560 is taken.
## Each cow is given a screening test for brucellosis which has a
## sensitivity of 96% and a specificity of 89%. Of the 150 cows tested
## 23 were positive to the screening test. What is the estimated prevalence
## of brucellosis in this herd (and its 95% confidence interval)?

epi.prev(pos = 23, tested = 150, se = 0.96, sp = 0.89, method = "blaker",
   units = 100, conf.level = 0.95)

## The estimated true prevalence of brucellosis in this herd is 5.1 cases per
## 100 cows (95% CI 0 -- 13 cases per 100 cows).
```

```
## Moujaber et al. (2008) analysed the seroepidemiology of Helicobacter pylori
## infection in Australia. They reported seroprevalence rates together with
## 95% confidence intervals by age group using the Clopper-Pearson exact
## method (Clopper and Pearson, 1934). The ELISA test they applied had 96.4%
## sensitivity and 92.7% specificity. A total of 151 subjects 1 -- 4 years
## of age were tested. Of this group 6 were positive. What is the estimated
## true prevalence of Helicobacter pylori in this age group?

epi.prev(pos = 6, tested = 151, se = 0.964, sp = 0.927, method = "c-p",
   units = 100, conf.level = 0.95)

## The estimated true prevalence of Helicobacter pylori in 1 -- 4 year olds is
## 0 cases per 100 (95% 0 -- 1.3 cases per 100).

## Three dairy herds are tested for tuberculosis. On each herd a different test
## regime is used (each with a different diagnostic test sensitivity and
## specificity). The number of animals tested in each herd were 210, 189 and
## 124, respectively. The number of test-positives in each herd were 8, 12
## and 7. Test sensitivities were 0.60, 0.65 and 0.70 (respectively). Test
## specificities were 0.90, 0.95 and 0.99. What is the estimated true
## prevalence of tuberculosis in the three herds?

rval <- epi.prev(pos = c(8,12,7), tested = c(210,189,124),
   se = c(0.60,0.65,0.70), sp = c(0.90,0.95,0.99), method = "blaker",
   units = 100, conf.level = 0.95)
round(rval$tp, digits = 3)

## True prevalence estimates for each herd:
## Herd 1: 0.00 (95% CI 0.00 to 2.05) cases per 100 cows.
## Herd 2: 2.25 (95% CI 0.00 to 9.45) cases per 100 cows.
## Herd 3: 6.73 (95% CI 0.99 to 9.00) cases per 100 cows.
```

`epi.propsize` *Sample size, power and minimum detectable risk ratio when comparing proportions*

Description

Calculates the sample size, power or minimum detectable risk ratio when comparing proportions.

Usage

```
epi.propsize(treat, control, n, power, r = 1, design = 1,
   sided.test = 2, conf.level = 0.95)
```

Arguments

treat	the expected proportion for the treatment group (see below).
control	the expected proportion for the control group (see below).
n	scalar, defining the total number of subjects in the study (i.e. the number in the treatment plus the number in the control group).
power	scalar, the required study power.
r	scalar, the number in the treatment group divided by the number in the control group.
design	scalar, the estimated design effect.
sided.test	use a one- or two-sided test? Use a two-sided test if you wish to evaluate whether or not the treatment group is better or worse than the control group. Use a one-sided test to evaluate whether or not the treatment group is better than the control group.
conf.level	scalar, defining the level of confidence in the computed result.

Details

The methodology in this function follows the approach described in Chapter 8 of Woodward (2005).

With this function it is assumed that one of the two proportions is known and we want to test the null hypothesis that the second proportion is equal to the first. Users are referred to the epi.cohortsize function which relates to the two-sample problem where neither proportion is known (or assumed, at least).

Because there is much more uncertainty in the two sample problem where neither proportion is known, epi.cohortsize returns much larger sample size estimates. This function (epi.propsize) should be used in particular situations such as when a politician claims that at least 90% of the population use seatbelts and we want to see if the data supports this claim.

Value

A list containing the following:

n.total	the total number of subjects required for the specified level of confidence and power, respecting the requirement for r times as many individuals in the treatment group compared with the control group.
n.treat	the total number of subjects in the treatment group for the specified level of confidence and power, respecting the requirement for r times as many individuals in the treatment group compared with the control group.
n.control	the total number of subjects in the control group for the specified level of confidence and power, respecting the requirement for r times as many individuals in the treatment group compared with the control group.
power	the power of the study given the number of study subjects, the expected effect size and level of confidence.
lambda	the proportion in the treatment group divided by the proportion in the control group (a risk ratio).

Note

The power of a study is its ability to demonstrate the presence of an association, given that an association actually exists.

Values need to be entered for `control`, `n`, and `power` to return a value for `lambda`. In this situation, the lower value of lambda represents the maximum detectable risk ratio that is less than 1; the upper value of lambda represents the minimum detectable risk ratio greater than 1.

References

Fleiss JL (1981). Statistical Methods for Rates and Proportions. Wiley, New York.

Kelsey JL, Thompson WD, Evans AS (1986). Methods in Observational Epidemiology. Oxford University Press, London, pp. 254 - 284.

Woodward M (2005). Epidemiology Study Design and Data Analysis. Chapman & Hall/CRC, New York, pp. 381 - 426.

Examples

```
## EXAMPLE 1 (from Woodward 2005 pp. 403 - 404):
## A government initiative has decided to reduce the prevalence of male
## smoking to, at most, 30%. A sample survey is planned to test, at the
## 0.05 level, the hypothesis that the percentage of smokers in the male
## population is 30% against the one-sided alternative that it is greater.
## The survey should be able to find a prevalence of 32%, when it is true,
## with 0.90 power. How many men need to be sampled?

epi.propsize(treat = 0.30, control = 0.32, n = NA, power = 0.90,
   r = 1, design = 1, sided.test = 1, conf.level = 0.95)

## ## A total of 18,316 men should be sampled: 9158 in the treatment group and
## 9158 in the control group. The risk ratio (that is, the prevalence of
## smoking in males post government initiative divided by the prevalence of
## smoking in males pre inititative is 0.94.


## EXAMPLE 2:
## If we sample only 10,000 men (5000 in the treatment group and 5000 in the
## control group) what is the maximum detectable risk ratio that is less
## than 1?

epi.propsize(treat = NA, control = 0.32, n = 10000, power = 0.90,
   r = 1, design = 1, sided.test = 1, conf.level = 0.95)

## If we sample only 10,000 men the maximum detectable risk ratio will be 0.91.
```

epi.RtoBUGS *R to WinBUGS data conversion*

Description

Writes data from an R list to a text file in WinBUGS-compatible format.

Usage

```
epi.RtoBUGS(datalist, towhere)
```

Arguments

datalist	a list (normally, with named elements) which may include scalars, vectors, matrices, arrays of any number of dimensions, and data frames.
towhere	a character string identifying where the file is to be written.

Details

The function doesn't check to ensure that only numbers are being produced. In particular, factor labels in a dataframe will be output to the file, which normally won't be desired.

Author(s)

Terry Elrod (terry.elrod@ualberta.ca), Kenneth Rice.

References

Best, NG. WinBUGS 1.3.1 Short Course, Brisbane, November 2000.

epi.SClip *Lip cancer in Scotland 1975 - 1980*

Description

This data set provides counts of lip cancer diagnoses made in Scottish districts from 1975 to 1980. In addition to district-level counts of disease events and estimates of the size of the population at risk, the data set contains (for each district) an estimate of the percentage of the population involved in outdoor industry (agriculture, fishing, and forestry). It is known that exposure to sunlight is a risk factor for cancer of the lip and high counts are to be expected in districts where there is a high proportion of the workforce involved in outdoor industry.

Usage

```
data(epi.SClip)
```

Format

A data frame with 56 observations on the following 6 variables.

gridcode alternative district identifier.

id numeric district identifier (1 to 56).

district district name.

cases number of lip cancer cases diagnosed 1975 - 1980.

population total person years at risk 1975 - 1980.

prop.ag percent of the population engaged in outdoor industry.

Source

This data set has been analysed by a number of authors including Clayton and Kaldor (1987), Conlon and Louis (1999), Stern and Cressie (1999), and Carlin and Louis (2000, p 270).

References

Clayton D, Kaldor J (1987). Empirical Bayes estimates of age-standardized relative risks for use in disease mapping. Biometrics 43: 671 - 681.

Conlon EM, Louis TA (1999). Addressing multiple goals in evaluating region-specific risk using Bayesian methods. In: Lawson AB (Editor), Disease Mapping and Risk Assessment for Public Health. John Wiley & Sons, Ltd, Chichester, pp. 31 - 47.

Stern H, Cressie N (1999). Inference in extremes in disease mapping. In: Lawson AB (Editor), Disease Mapping and Risk Assessment for Public Health. John Wiley & Sons, Ltd, Chichester, pp. 63 - 84.

Carlin BP, Louis TA (2000). Bayes and Empirical Bayes Methods for Data Analysis - Monographs on Statistics and Applied Probability 69. Chapman and Hall, London, pp. 270.

---

epi.simplesize *Sample size under simple random sampling*

Description

Estimates the required sample size under under simple random sampling.

Usage

```
epi.simplesize(N = 1E+06, Vsq, Py, epsilon.r, method = "mean",
   conf.level = 0.95)
```

Arguments

N	scalar, representing the population size.
Vsq	scalar, if method is total or mean this is the relative variance of the variable to be estimated (i.e. var/mean^2).
Py	scalar, if method is proportion this is an estimate of the unknown population proportion.
epsilon.r	the maximum relative difference between our estimate and the unknown population value.
method	a character string indicating the method to be used. Options are total, mean, or proportion.
conf.level	scalar, defining the level of confidence in the computed result.

Value

Returns an integer defining the size of the sample is required.

Note

epsilon.r defines the maximum relative difference between our estimate and the unknown population value. The sample estimate should not differ in absolute value from the true unknown population parameter d by more than epsilon.r * d.

References

Levy PS, Lemeshow S (1999). Sampling of Populations Methods and Applications. Wiley Series in Probability and Statistics, London, pp. 70 - 75.

Scheaffer RL, Mendenhall W, Lyman Ott R (1996). Elementary Survey Sampling. Duxbury Press, New York, pp. 95.

Otte J, Gumm I (1997). Intra-cluster correlation coefficients of 20 infections calculated from the results of cluster-sample surveys. Preventive Veterinary Medicine 31: 147 - 150.

Examples

```
## EXAMPLE 1:
## A city contains 20 neighbourhood health clinics and it is desired to take a
## sample of clinics to estimate the total number of persons from all these
## clinics who have been given, during the past 12 month period, prescriptions
## for a recently approved antidepressant. If we assume that the average number
## of people seen at these clinics is 1500 per year with the standard deviation
## equal to 300, and that approximately 5% of patients (regardless of clinic)
## are given this drug, how many clinics need to be sampled to yield an estimate
## that is within 20% of the true population value?

pmean <- 1500 * 0.05; pvar <- (300 * 0.05)^2
epi.simplesize(N = 20, Vsq = (pvar / pmean^2), Py = NA, epsilon.r = 0.20,
   method = "total", conf.level = 0.95)

## Three clinics need to be sampled to meet the survey requirements.
```

```
## EXAMPLE 2:
## We want to estimate the mean bodyweight of deer on a farm. There are 278
## animals present. We anticipate the mean body weight to be around 200 kg
## and the standard deviation of body weight to be 30 kg. We would like to
## be 95% certain that our estimate is within 10 kg of the true mean. How
## many deer should be sampled?

epi.simplesize(N = 278, Vsq = 30^2 / 200^2, Py = NA, epsilon.r = 10/200,
   method = "mean", conf.level = 0.95)

## A total of 31 deer need to be sampled to meet the survey requirements.

## EXAMPLE 3:
## We want to estimate the seroprevalence of Brucella abortus in a population
## of cattle. An estimate of the unknown prevalence of B. abortus in this
## population is 0.15. We would like to be 95% certain that our estimate is
## within 20% of the true proportion of the population that is seropositive
## to B. abortus. Calculate the required sample size.

n.crude <- epi.simplesize(N = 1E+06, Vsq = NA, Py = 0.15, epsilon.r = 0.20,
   method = "proportion", conf.level = 0.95)
n.crude

## A total of 544 cattle need to be sampled to meet the survey requirements.

## EXAMPLE 3 (continued):
## Being seropositive to brucellosis is likely to cluster within herds.
## Otte and Gumm (1997) cite the intraclass correlation coefficient (rho) of
## Brucella abortus to be in the order of 0.09. Adjust the sample size
## estimate to account for clustering at the herd level. Assume that, on
## average, 20 animals will be sampled per herd:

## Let D equal the design effect and nbar equal the average number of
## individuals per cluster:

## rho = (D - 1) / (nbar - 1)

## Solving for D:
## D <- rho * (nbar - 1) + 1

rho <- 0.09; nbar <- 20
D <- rho * (nbar - 1) + 1

n.adj <- ceiling(n.crude * D)
n.adj

## After accounting for the presence of clustering at the herd level we
## estimate that a total of 1475 cattle need to be sampled to meet
## the requirements of the survey.
```

`epi.smd` *Fixed-effect meta-analysis of continuous outcomes using the standardised mean difference method*

Description

Computes the standardised mean difference and confidence intervals of the standardised mean difference for continuous outcome data.

Usage

```
epi.smd(mean.trt, sd.trt, n.trt, mean.ctrl, sd.ctrl, n.ctrl,
   names, method = "cohens", conf.level = 0.95)
```

Arguments

`mean.trt`	a vector, defining the mean outcome in the treatment group.
`sd.trt`	a vector, defining the standard deviation of the outcome in the treatment group.
`n.trt`	a vector, defining the number of subjects in the treatment group.
`mean.ctrl`	a vector, defining the mean outcome in the control group.
`sd.ctrl`	a vector, defining the standard deviation of the outcome in the control group.
`n.ctrl`	a vector, defining the number of subjects in the control group.
`names`	character string identifying each trial.
`method`	a character string indicating the method to be used. Options are `cohens` or `hedges` and `glass`.
`conf.level`	magnitude of the returned confidence interval. Must be a single number between 0 and 1.

Value

A list containing the following:

`md`	standardised mean difference and its confidence interval computed for each trial.
`md.invar`	the inverse variance (fixed effects) summary standardised mean difference.
`md.dsl`	the DerSimonian and Laird (random effects) summary standardised mean difference.
`heterogeneity`	a vector containing `Q` the heterogeneity test statistic, `df` the degrees of freedom and its associated P-value.

Note

The standardised mean difference method is used when trials assess the same outcome, but measure it in a variety of ways. For example: a set of trials might measure depression scores in psychiatric patients but use different methods to quantify depression. In this circumstance it is necessary to standardise the results of the trials to a uniform scale before they can be combined. The standardised mean difference method expresses the size of the treatment effect in each trial relative to the variability observed in that trial.

References

Deeks JJ, Altman DG, Bradburn MJ (2001). Statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. In: Egger M, Davey Smith G, Altman D (eds). Systematic Review in Health Care Meta-Analysis in Context. British Medical Journal, London, pp. 290 - 291.

See Also

epi.dsl, epi.iv, epi.mh

Examples

```
## EXAMPLE 1:
## A systematic review comparing assertive community treatment (ACT) for the
## severely mentally ill was compared to standard care. A systematic review
## comparing ACT to standard care found three trials that assessed mental
## status after 12 months. All three trials used a different scoring system,
## so standardisation is required before they can be compared.

names <- c("Audini", "Morse", "Lehman")
mean.trt <- c(41.4, 0.95, -4.10)
mean.ctrl <- c(42.3, 0.89, -3.80)
sd.trt <- c(14, 0.76, 0.83)
sd.ctrl <- c(12.4, 0.65, 0.87)
n.trt <- c(30, 37, 67)
n.ctrl <- c(28, 35, 58)

epi.smd(mean.trt, sd.trt, n.trt, mean.ctrl, sd.ctrl, n.ctrl,
   names, method = "cohens", conf.level = 0.95)
```

---

epi.stratasize *Sample size under under stratified random sampling*

Description

Estimates the required sample size under under stratified random sampling.

Usage

```
epi.stratasize(strata.n, strata.mean, strata.var, strata.Py, epsilon.r,
   method = "mean", conf.level = 0.95)
```

Arguments

strata.n	vector, defining the size of each strata.
strata.mean	vector, representing the expected means in each strata. Only used when method = "mean", "total" or "pps".

strata.var	vector, representing the expected variance in each strata. Only used when method = "mean", "total" or "pps".
strata.Py	vector, representing the expected proportions in each strata. Only used when method = "proportion".
epsilon.r	the maximum relative difference between our estimate and the unknown population value.
method	a character string indicating the method to be used. Options are mean, total, proportion, or pps.
conf.level	scalar, defining the level of confidence in the computed result.

Value

A list containing the following:

strata.sample	the estimated sample size for each strata.
strata.total	the estimated total size.
strata.stats	mean the mean across all strata, sigma.bx the among-strata variance, sigma.wx the within-strata variance, and sigma.x the among-strata variance plus the within-strata variance, rel.var the within-strata variance divided by the square of the mean, and gamma the ratio of among-strata variance to within-strata variance.

Note

Use method proportion to estimate sample size using stratified random sampling with equal weights (see Levy and Lemeshow, page 176). Use method pps to estimate sample size using proportional stratified random sampling with proportional allocation (see Levy and Lemeshow, page 179).

When method = "proportion" the vectors strata.mean and strata.var are ignored.

Author(s)

Mark Stevenson (Faculty of Veterinary and Agricultural Sciences, The University of Melbourne, Australia).

Javier Sanchez (Atlantic Veterinary College, University of Prince Edward Island, Charlottetown Prince Edward Island, C1A 4P3, Canada).

References

Levy PS, Lemeshow S (1999). Sampling of Populations Methods and Applications. Wiley Series in Probability and Statistics, London, pp. 175 - 179.

Examples

```
## EXAMPLE 1:
## Hospital episodes (Levy and Lemeshow 1999, page 176 -- 178)
## We plan to take a sample of the members of a health maintenance
## organisation (HMO) for purposes of estimating the average number
## of hospital episodes per person per year. The sample will be selected
```

```
## from membership lists according to age (under 45 years, 45 -- 64 years,
## 65 years and over). The number of members in each strata are 600, 500,
## and 400 (respectively). Previous data estimates the mean number of
## hospital episodes per year for each strata as 0.164, 0.166, and 0.236
## (respectively). The variance of these estimates are 0.245, 0.296, and
## 0.436 (respectively). How many from each strata should be sampled to be
## 95% that the sample estimate of hospital episodes is within 20% of the
## true value?

strata.n <- c(600, 500, 400)
strata.mean <- c(0.164, 0.166, 0.236)
strata.var <- c(0.245, 0.296, 0.436)
epi.stratasize(strata.n, strata.mean, strata.var, strata.Py,
   epsilon.r = 0.20, method = "mean", conf.level = 0.95)

## The number allocated to the under 45 years, 45 -- 64 years, and 65 years
## and over stratums should be 223, 186, and 149 (a total of 558). These
## results differ from the worked example provided in Levy and Lemeshow where
## certainty is set to approximately 99%.

## EXAMPLE 2:
## Dairies are to be sampled to determine the proportion of herd managers
## using foot bathes. Herds are stratified according to size (small, medium,
## and large). The number of herds in each strata are 1500, 2500, and 4000
## (respectively). A review of the literature indicates that use of foot bathes
## on farms is in the order of 0.50, with the probability of usage increasing
## as herds get larger. How many dairies should be sampled?

strata.n <- c(1500, 2500, 4000)
strata.Py <- c(0.50, 0.60, 0.70)
epi.stratasize(strata.n, strata.mean, strata.var, strata.Py,
   epsilon.r = 0.20, method = "proportion", conf.level = 0.95)

## A total of 54 herds should be sampled: 10 small, 17 medium, and 27 large.
```

`epi.supb` *Estimate the sample size for a parallel superiority trial, binary outcomes*

Description

Computes the sample size for a parallel superiority trial with a binary outcome variable.

Usage

```
epi.supb(treat, control, delta, n, r = 1, power, alpha)
```

Arguments

treat	the expected proportion of successes in the treatment group.
control	the expected proportion of successes in the control group.
delta	the equivalence limit, expressed as a proportion.
n	scalar, the total number of study subjects in the trial.
r	scalar, the number in the treatment group divided by the number in the control group.
power	scalar, the required study power.
alpha	scalar, defining the desired alpha level.

Value

A list containing one or more of the following:

n.treat	the required number of study subject in the treatment group.
n.control	the required number of study subject in the control group.
n.total	the total number of study subjects required.

Note

Consider a clinical trial comparing two groups, a standard treatment (s) and a new treatment (n). In each group, a proportion of subjects respond to the treatment: Ps and Pn.

With a superiority trial we specify the maximum acceptable difference between Pn and Ps as delta. The null hypothesis is H0: Pn - Ps <= delta and the alternative hypothesis is H1: Pn - Ps > delta.

An equivalence trial is used if want to prove that two treatments produce the same clinical outcomes. With an equivalence trial, we specify the maximum acceptable difference between Pn and Ps as delta. The null hypothesis is H0: |Ps - Pn| >= delta and the alternative hypothesis is H1: |Ps - Pn| < delta. In bioequivalence trials, a 90% confidence interval is often used. The value of the maximum acceptable difference delta is chosen so that a patient will not detect any change in effect when replacing the standard treatment with the new treatment.

With a non-inferiority trial, we specify the maximum acceptable difference between Pn and Ps as delta. The null hypothesis is H0: Ps - Pn >= delta and the alternative hypothesis is H1: Ps - Pn < delta. The aim of a non-inferiority trial is show that a new treatment is not (much) inferior to a standard treatment. Showing non-inferiority can be of interest because: (a) it is often not ethically possible to do a placebo-controlled trial, (b) the new treatment is not expected to be better than the standard treatment on primary efficacy endpoints, but is safer, (c) the new treatment is not expected to be better than the standard treatment on primary efficacy endpoints, but is cheaper to produce or easier to administer, (d) the new treatment is not expected to be better than the standard treatment on primary efficacy endpoints in clinical trial, but compliance will be better outside the clinical trial and hence efficacy better outside the trial.

For a summary of the key features of superiority, equivalence and non-inferiority trials, refer to the documentation for epi.equivb.

When calculating the power of a study, note that the variable n refers to the total study size (that is, the number of subjects in the treatment group plus the number in the control group).

References

Chow S, Shao J, Wang H (2008). Sample Size Calculations in Clinical Research. Chapman & Hall/CRC Biostatistics Series, page 90.

Julious SA (2004). Sample sizes for clinical trials with normal data. Statistics in Medicine 23: 1921 - 1986.

Pocock SJ (1983). Clinical Trials: A Practical Approach. Wiley, New York.

Examples

```
## EXAMPLE 1 (from Chow S, Shao J, Wang H 2008, p. 90):
## Suppose that a pharmaceutical company is interested in conducting a
## clinical trial to compare the efficacy of two antimicrobial agents
## when administered orally once daily in the treatment of patients
## with skin infections. In what follows, we consider the situation
## where the intended trial is for testing superiority of the
## test drug over the active control drug. For this purpose, the following
## assumptions are made. First, sample size calculation will be performed
## for achieving 80% power at the 5% level of significance.

## Assume the true mean cure rates of the treatment agents and the active
## control are 85% and 65%, respectively. Assume the superiority
## margin is 5%.

epi.supb(treat = 0.85, control = 0.65, delta = 0.05, n = NA,
   r = 1, power = 0.80, alpha = 0.05)

## A total of 196 subjects need to be enrolled in the trial, 98 in the
## treatment group and 98 in the control group.
```

`epi.supc` *Estimate the sample size for a parallel superiority trial, continuous outcomes*

Description

Computes the sample size for a parallel superiority trial with a continuous outcome variable.

Usage

```
epi.supc(treat, control, sd, delta, n, r = 1, power, alpha)
```

Arguments

`treat`	the expected mean of the outcome of interest in the treatment group.
`control`	the expected mean of the outcome of interest in the control group.
`sd`	the expected population standard deviation of the outcome of interest.

delta	the equivalence limit, expressed as a proportion.
n	scalar, the total number of study subjects in the trial.
r	scalar, the number in the treatment group divided by the number in the control group.
power	scalar, the required study power.
alpha	scalar, defining the desired alpha level.

Value

A list containing one or more of the following:

n.treat	the required number of study subject in the treatment group.
n.control	the required number of study subject in the control group.
n.total	the total number of study subjects required.

Note

Consider a clinical trial comparing two groups, a standard treatment (s) and a new treatment (n). In each group, a proportion of subjects respond to the treatment: Ps and Pn.

With a superiority trial we specify the maximum acceptable difference between Pn and Ps as delta. The null hypothesis is H0: Pn - Ps <= delta and the alternative hypothesis is H1: Pn - Ps > delta.

An equivalence trial is used if want to prove that two treatments produce the same clinical outcomes. With an equivalence trial, we specify the maximum acceptable difference between Pn and Ps as delta. The null hypothesis is H0: |Ps - Pn| >= delta and the alternative hypothesis is H1: |Ps - Pn| < delta. In bioequivalence trials, a 90% confidence interval is often used. The value of the maximum acceptable difference delta is chosen so that a patient will not detect any change in effect when replacing the standard treatment with the new treatment.

With a non-inferiority trial, we specify the maximum acceptable difference between Pn and Ps as delta. The null hypothesis is H0: Ps - Pn >= delta and the alternative hypothesis is H1: Ps - Pn < delta. The aim of a non-inferiority trial is show that a new treatment is not (much) inferior to a standard treatment. Showing non-inferiority can be of interest because: (a) it is often not ethically possible to do a placebo-controlled trial, (b) the new treatment is not expected to be better than the standard treatment on primary efficacy endpoints, but is safer, (c) the new treatment is not expected to be better than the standard treatment on primary efficacy endpoints, but is cheaper to produce or easier to administer, (d) the new treatment is not expected to be better than the standard treatment on primary efficacy endpoints in clinical trial, but compliance will be better outside the clinical trial and hence efficacy better outside the trial.

For a summary of the key features of superiority, equivalence and non-inferiority trials, refer to the documentation for epi.equivb.

When calculating the power of a study, note that the variable n refers to the total study size (that is, the number of subjects in the treatment group plus the number in the control group).

References

Chow S, Shao J, Wang H (2008). Sample Size Calculations in Clinical Research. Chapman & Hall/CRC Biostatistics Series, page 61.

Julious SA (2004). Sample sizes for clinical trials with normal data. Statistics in Medicine 23: 1921 - 1986.

Pocock SJ (1983). Clinical Trials: A Practical Approach. Wiley, New York.

Examples

```
## EXAMPLE 1
## A pharmaceutical company is interested in conducting a clinical trial
## to compare two cholesterol lowering agents for treatment of patients with
## congestive heart disease (CHD) using a parallel design. The primary
## efficacy parameter is the concentration of high density lipoproteins.
## (HDL). We consider the situation where the intended trial is to test
## superiority of the test drug over the active control agent. Sample
## size calculations are to be calculated to achieve 80% power at the
## 5% level of significance.

## In this example, we assume that if treatment results in a 5 unit
## (i.e. delta = 5) increase in HDL it is declared to be superior to the
## active control. Assume the standard deviation of HDL is 10 units and
## the HDL concentration in the treatment group is 20 units and the
## HDL concentration in the control group is 20 units.

epi.supc(treat = 20, control = 20, sd = 10, delta = 5, n = NA,
   r = 1, power = 0.80, alpha = 0.05)

## A total of 100 subjects need to be enrolled in the trial, 50 in the
## treatment group and 50 in the control group.
```

---

epi.survivalsize *Sample size, power and minimum detectable hazard for time to event studies*

Description

Computes the sample size, power or minimum detectable hazard when comparing survival (time to event).

Usage

```
epi.survivalsize(treat, control, n, power, r = 1, design = 1,
   sided.test = 2, conf.level = 0.95)
```

Arguments

treat	the expected value for the treatment group (see below).
control	the expected value for the control group (see below).
n	scalar, defining the total number of subjects in the study (i.e. the number in the treatment and control group).
power	scalar, the required study power.
r	scalar, the number in the treatment group divided by the number in the control group. This argument is ignored when method = "proportions".
design	scalar, the estimated design effect.
sided.test	use a one- or two-sided test? Use a two-sided test if you wish to evaluate whether or not the treatment group is better or worse than the control group. Use a one-sided test to evaluate whether or not the treatment group is better than the control group.
conf.level	scalar, defining the level of confidence in the computed result.

Details

The argument treat is the proportion of treated subjects that will have not experienced the event of interest at the end of the study period and control is the proportion of control subjects that will have not experienced the event of interest at the end of the study period. See Therneau and Grambsch pp 61 - 65.

Value

A list containing one or more of the following:

n.crude	the crude estimated total number of subjects required for the specified level of confidence and power.
n.total	the total estimated number of subjects required for the specified level of confidence and power, respecting the requirement for r times as many individuals in the treatment group compared with the control group.
hazard	the minimum detectable hazard ratio >1 and the maximum detectable hazard ratio <1.
power	the power of the study given the number of study subjects, the expected hazard ratio and level of confidence.

Note

The power of a study is its ability to demonstrate the presence of an association, given that an association actually exists.

References

Therneau TM, Grambsch PM (2000). Modelling Survival Data - Extending the Cox Model. Springer, London, pp. 61 - 65.

Woodward M (2005). Epidemiology Study Design and Data Analysis. Chapman & Hall/CRC, New York, pp. 381 - 426.

Examples

```
## EXAMPLE 1 (from Therneau and Grambsch 2000 p. 63):
## The 5-year survival probability of patients receiving a standard treatment
## is 0.30 and we anticipate that a new treatment will increase it to 0.45.
## Assume that a study will use a two-sided test at the 0.05 level with 0.90
## power to detect this difference. How many events are required?

epi.survivalsize(treat = 0.45, control = 0.30, n = NA, power = 0.90,
   r = 1, design = 1, sided.test = 2, conf.level = 0.95)

## A total of 250 events are required. Assuming one event per individual,
## assign 125 individuals to the treatment group and 125 to the control group.


## EXAMPLE 2 (from Therneau and Grambsch 2000 p. 63):
## What is the minimum detectable hazard in a study involving 500 subjects where
## the treatment to control ratio is 1:1, assuming a power of 0.90 and a
## 2-sided test at the 0.05 level?

epi.survivalsize(treat = NA, control = NA, n = 500, power = 0.90,
   r = 1, design = 1, sided.test = 2, conf.level = 0.95)

## Assuming treatment increases time to event (compared with controls), the
## minimum detectable hazard of a study involving 500 subjects (250 in the
## treatment group and 250 in the controls) is 1.33.
```

---

epi.tests *Sensitivity, specificity and predictive value of a diagnostic test*

Description

Computes true and apparent prevalence, sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios from count data provided in a 2 by 2 table.

Usage

```
epi.tests(dat, conf.level = 0.95)

## S3 method for class 'epi.tests'
print(x, ...)

## S3 method for class 'epi.tests'
summary(object, ...)
```

Arguments

dat	an object of class table containing the individual cell frequencies (see below).
conf.level	magnitude of the returned confidence interval. Must be a single number between 0 and 1.

`x, object`	an object of class `epi.tests`.
`...`	Ignored.

Details

Exact binomial confidence limits are calculated for test sensitivity, specificity, and positive and negative predictive value (see Collett 1999 for details).

Confidence intervals for positive and negative likelihood ratios are based on formulae provided by Simel et al. (1991).

Diagnostic accuracy is defined as the proportion of all tests that give a correct result. Diagnostic odds ratio is defined as how much more likely will the test make a correct diagnosis than an incorrect diagnosis in patients with the disease (Scott et al. 2008). The number needed to diagnose is defined as the number of paitents that need to be tested to give one correct positive test. Youden's index is the difference between the true positive rate and the false positive rate. Youden's index ranges from -1 to +1 with values closer to 1 if both sensitivity and specificity are high (i.e. close to 1).

Value

An object of class `epi.tests` containing the following:

`aprev`	apparent prevalence.
`tprev`	true prevalence.
`se`	test sensitivity.
`sp`	test specificity.
`diag.acc`	diagnostic accuracy.
`diag.or`	diagnostic odds ratio.
`nnd`	number needed to diagnose.
`youden`	Youden's index.
`ppv`	positive predictive value.
`npv`	negative predictive value.
`plr`	likelihood ratio of a positive test.
`nlr`	likelihood ratio of a negative test.

Note

	Disease +	Disease -	Total
Test +	a	b	a+b
Test -	c	d	c+d
Total	a+c	b+d	a+b+c+d

Author(s)

Mark Stevenson (Faculty of Veterinary and Agricultural Sciences, The University of Melbourne, Australia).

References

Altman DG, Machin D, Bryant TN, and Gardner MJ (2000). Statistics with Confidence, second edition. British Medical Journal, London, pp. 28 - 29.

Bangdiwala SI, Haedo AS, Natal ML (2008). The agreement chart as an alternative to the receiver-operating characteristic curve for diagnostic tests. Journal of Clinical Epidemiology 61: 866 - 874.

Collett D (1999). Modelling Binary Data. Chapman & Hall/CRC, Boca Raton Florida, pp. 24.

Scott IA, Greenburg PB, Poole PJ (2008). Cautionary tales in the clinical interpretation of studies of diagnostic tests. Internal Medicine Journal 38: 120 - 129.

Simel D, Samsa G, Matchar D (1991). Likelihood ratios with confidence: Sample size estimation for diagnostic test studies. Journal of Clinical Epidemiology 44: 763 - 770.

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Examples

```
## Scott et al. 2008, Table 1:
## A new diagnostic test was trialled on 1586 patients. Of 744 patients
## that were disease positive, 670 tested positive. Of 842 patients that
## were disease negative, 640 tested negative. What is the likeliood
## ratio of a positive test? What is the number needed to diagnose?

dat <- as.table(matrix(c(670,202,74,640), nrow = 2, byrow = TRUE))
colnames(dat) <- c("Dis+","Dis-")
rownames(dat) <- c("Test+","Test-")
rval <- epi.tests(dat, conf.level = 0.95)
print(rval); summary(rval)

## Test sensitivity is 0.90 (95% CI 0.88 -- 0.92). Test specificity is
## 0.76 (95% CI 0.73 -- 0.79). The likelihood ratio of a positive test
## is 3.75 (95% CI 3.32 to 4.24). The number needed to diagnose is
## 1.51 (95% CI 1.41 to 1.65). Around 15 persons need to be tested
## to return 10 positive tests.
```

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