Package: epiR (via r-universe)

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Title Tools for the Analysis of Epidemiological Data

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Description Tools for the analysis of epidemiological and surveillance 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, computation of confidence intervals around incidence risk and incidence rate estimates and sample size calculations for cross-sectional, case-control and cohort studies. Surveillance tools include functions to calculate an appropriate sample size for 1- and 2-stage representative freedom surveys, functions to estimate surveillance system sensitivity and functions to support scenario tree modelling analyses.

Depends R (>= 3.0.0), survival

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Suggests MASS (>= 3.1-20), dplyr, foreign, ggplot2, knitr, rmarkdown, bookdown, plyr, RColorBrewer, scales, sp, spData (>= 2.3.0), spatstat, tidyr

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`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", elab = NA, olab = NA, digits = 2,
   conf.level = 0.95, units = 100, interpret = FALSE, outcome = "as.columns")

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

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

Arguments

`dat`	a vector of length four, an object of class `table` or an object of class `grouped_df` from package `dplyr` containing the individual cell frequencies (see below).

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.
elab	character string, setting the label for the exposure variable.
olab	character string, setting the label for the outcome variable.
digits	scalar, number of digits to be reported for print output. Must be an integer of either 2, 3 or 4.
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.
interpret	logical. If TRUE interpretive statements are appended to the printepi.2by2 object.
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
Exposure +	a	b	a+b
Exposure -	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
Exposure +	a	b
Exposure -	c	d
Total	a + c	b + d

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.
`interp`	logical. Are interpretative statements included?
`units`	character string listing the outcome measure units.
`tab`	a data frame comprised of of the contingency table data.
`massoc.summary`	a data frame listing the computed measures of association, measures of effect in the exposed and measures of effect in the population and their confidence intervals.
`massoc.interp`	a data frame listing the interpretive statements for each computed measure of association.
`massoc.detail`	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.

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

`RR`	Wald, Taylor, score and Koopman point estimates and confidence intervals for the incidence risk ratios for each strata. Wald, Taylor, score and Koopman 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 point estimates and confidence intervals for the odds ratios for each strata. Wald, score, Cornfield and maximum likelihood point estimates and confidence intervals for the crude odds ratio. Wald point estimate and confidence interval for the Mantel-Haenszel adjusted odds ratio.
`ARisk`	Wald and score point estimates and confidence intervals for the attributable risk (risk difference) for each strata. Wald and score point estimates and confidence intervals for the crude attributable risk. Wald, Sato and Greenland-Robins point estimates and confidence intervals for the Mantel-Haenszel adjusted attributable risk.
`NNT`	Wald and score point estimates and confidence intervals for the number needed to treat for benefit (NNTB) or number needed to treat for harm (NNTH).
`PARisk`	Wald and Pirikahu point estimates and confidence intervals for the population attributable risk for each strata. Wald and Pirikahu point estimates and confidence intervals for the crude population attributable risk. The Pirikahu confidence intervals are calculated using the delta method.
`AFRisk`	Wald point estimates and confidence intervals for the attributable fraction for each strata. Wald point estimates and confidence intervals for the crude attributable fraction.

PAFRisk — Wald point estimates and confidence intervals for the population attributable fraction for each strata. Wald point estimates and confidence intervals for the crude population attributable fraction.

E — E-value point estimates and confidence intervals for each strata. E-value point estimate and confidence interval for the crude incidence risk ratio. E-value point estimate and confidence interval for the Mantel-Haenszel adjusted incidence risk ratio.

wald.rr — Wald test where the null hypothesis is that the true strata incidence risk ratios are equal to unity. Wald test where the null hypothesis is that the true crude incidence risk ratio is equal to unity.

wald.or — Wald test where the null hypothesis is that the true strata incidence odds ratios are equal to unity. Wald test where the null hypothesis is that the true crude incidence odds ratio is equal to unity.

chisq.strata — chi-squared test for a difference in exposed and non-exposed proportions for each strata.

chisq.crude — chi-squared test for a difference in exposed and non-exposed proportions across all strata.

chisq.mh — Mantel-Haenszel chi-squared test that the combined odds ratio estimate is equal to 1.

RR.homog — Mantel-Haenszel (Woolf) test of homogeneity of the individual strata incidence risk ratios.

OR.homog — Mantel-Haenszel (Woolf) 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 point estimates and confidence intervals for the incidence rate ratios for each strata. Wald point estimate and confidence interval for the crude incidence rate ratio. Wald point estimate and confidence interval for the Mantel-Haenszel adjusted incidence rate ratio.

ARate — Wald point estimates and confidence intervals for the attributable rate for each strata. Wald point estimate and confidence interval for the crude attributable rate. Wald point estimate and confidence interval for the Mantel-Haenszel adjusted attributable rate.

PARate — Wald point estimates and confidence intervals for the population attributable rate for each strata. Wald point estimates and confidence intervals for the crude population attributable rate.

AFRate — Wald point estimates and confidence intervals for the attributable fraction for each strata. Wald point estimate and confidence interval for the crude attributable fraction.

PAFRate — Wald point estimates and confidence intervals for the population attributable fraction for each strata. Wald point estimate and confidence interval for the crude poulation attributable fraction.

wald.irr — Wald test where the null hypothesis is that the true strata incidence rate ratios are equal to unity. Wald test where the null hypothesis is that the true crude incidence rate ratio is equal to unity.

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 that the combined odds ratio estimate is equal to 1.

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

OR	Wald, score, Cornfield and maximum likelihood point estimates and confidence intervals for the odds ratios for each strata. Wald, score, Cornfield and maximum likelihood point estimates and confidence intervals for the crude odds ratio. Wald point estimate and confidence interval for the Mantel-Haenszel adjusted odds ratio.
ARisk	Wald and score point estimates and confidence intervals for the attributable risk for each strata. Wald and score point estimates and confidence intervals for the crude attributable risk. Wald, Sato and Greenland-Robins point estimates and confidence intervals for the Mantel-Haenszel adjusted attributable risk.
PARisk	Wald and Pirikahu point estimates and confidence intervals for the population attributable risk for each strata. Wald and Pirikahu point estimate and confidence intervals for the crude population attributable risk.
AFest	Wald point estimates and confidence intervals for the estimated attributable fraction for each strata. Wald point estimate and confidence interval for the crude estimated attributable fraction.
PAFest	Wald point estimates and confidence intervals for the population estimated attributable fraction for each strata. Wald point estimate and confidence interval for the crude population estimated attributable fraction.
E	E-value point estimates and confidence intervals for each strata. E-value point estimate and confidence interval for the crude odds ratio. E-value point estimate and confidence interval for the Mantel-Haenszel adjusted odds ratio.
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 that the combined odds ratio estimate is equal to 1.
OR.homog	Mantel-Haenszel (Woolf) 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, Taylor, score and Koopman point estimates and confidence intervals for the prevalence ratios for each strata. Wald, Taylor, score and Koopman point estimate and confidence interval for the crude prevalence ratio. Wald point estimate and confidence interval for the Mantel-Haenszel adjusted prevalence ratio.

OR	Wald, score, Cornfield and maximum likelihood point estimates and confidence intervals for the odds ratios for each strata. Wald, score, Cornfield and maximum likelihood point estimate and confidence interval for the crude odds ratio. Wald point estimate and confidence interval for the Mantel-Haenszel adjusted odds ratio.
ARisk	Wald and score point estimates and confidence intervals for the attributable risk for each strata. Wald and score point estimate and confidence interval for the crude attributable risk. Wald, Sato and Greenland-Robins point estimate and confidence interval for the Mantel-Haenszel adjusted attributable risk.
NNT	Wald and score point estimates and confidence intervals for the number needed to treat for benefit (NNTB) or number needed to treat for harm (NNTH).
PARisk	Wald and Pirikahu point estimates and confidence intervals for the population attributable risk for each strata. Wald and Pirikahu point estimate and confidence interval for the crude population attributable risk.
AFRisk	Wald point estimates and confidence intervals for the attributable fraction for each strata. Wald point estimate and confidence interval for the crude attributable fraction.
PAFRisk	Wald point estimates and confidence intervals for the population attributable fraction for each strata. Wald point estimate and confidence interval for the crude population attributable fraction.
E	E-value point estimates and confidence intervals for each strata. E-value point estimate and confidence interval for the crude prevalence risk ratio. E-value point estimate and confidence interval for the Mantel-Haenszel adjusted prevalence risk ratio.
wald.rr	Wald test where the null hypothesis is that the true strata prevalence risk ratios are equal to unity. Wald test where the null hypothesis is that the true crude prevalence risk ratio is equal to unity.
wald.or	Wald test where the null hypothesis is that the true strata prevalence odds ratios are equal to unity. Wald test where the null hypothesis is that the true crude prevalence odds ratio is equal to unity.
chisq.strata	chi-squared test for a difference in exposed and non-exposed proportions for each strata.
chisq.crude	chi-squared test for a difference in exposed and non-exposed proportions across all strata.
chisq.mh	Mantel-Haenszel chi-squared test that the combined odds ratio estimate is equal to 1.
PR.homog	Mantel-Haenszel (Woolf) test of homogeneity of the individual strata prevalence ratios.
OR.homog	Mantel-Haenszel (Woolf) 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.

Confidence intervals for the Cornfield (`cfield`) odds ratios are computed using the hypergeometric distribution and computation times can be slow when the cell frequencies are large. For this reason,

Cornfield confidence intervals are only calculated if the total number of cell frequencies is less than 500. Maximum likelihood estimates of the odds ratio and Fisher's exact test are only calculated when the cell frequency total is less than 2E09.

If the Haldane-Anscombe (Haldane 1940, Anscombe 1956) correction is applied (i.e., addition of 0.5 to each cell of the 2 by 2 table when at least one of the cell frequencies is zero) Cornfield (`cfield`) odds ratios are not computed.

Variable `phi.coef` equals the phi coefficient (Fleiss et al. 2003, Equation 6.2, p. 98) and is included with the output for each of the uncorrected chi-squared tests. This value can be used for argument `rho.cc` in `epi.sscc`. Refer to the documentation for `epi.sscc` for details.

The Mantel-Haenszel chi-squared test that the combined odds ratio estimate is equal to 1 uses a two-sided test without continuity correction.

Interpretive statements for NNTB and NNTH follow the approach described by Altman (1998). See the examples for details. Note that number needed to treat to benefit (NNTB) and number needed to treat to harm (NNTH) estimates are not computed when `method = "cohort.time"` or `method = "case.control"` because the attributable risk can't be calculated using these study designs.

E-values are computed using the individual strata odds ratio Wald confidence interval estimates, crude odds ratio Wald confidence interval estimates, and Mantel-Haenszel adjusted Wald confidence interval estimates, where appropriate. When `method = "case.control"` the function sets the `rare` argument in function `epi.evalue` (called by `epi.2by2`) to `TRUE` when the frequency of the outcome is less than 0.05. Users wanting more control over this argument are advised to call function `epi.evalue` directly.

`NAs` are returned for the e-value estimates when there are zero cell frequencies in one or more tables of a stratified analysis.

Note

For cohort studies where the outcome of interest is expressed as an incidence risk, measures of association include the incidence risk ratio and the incidence odds ratio. When the incidence of the outcome in the study population is low (less than 5%) the incidence odds ratio will provide a reliable estimate of the incidence risk ratio. The more frequent the outcome becomes, the more the incidence 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.

For cohort studies where outcome of interest is expressed as an incidence rate, the incidence rate ratio is used as a measure of association. For case-control studies the exposure odds ratio is used as a measure of association.

For cross-sectional studies where the outcome of interest is expressed as a prevalence, measures of association include the prevalence risk ratio and the prevalence odds ratio. When the prevalence of the outcome in the study population is low (less than 5%) the prevalence odds ratio will provide a reliable estimate of the incidence risk ratio. The more frequent the outcome becomes, the more the prevalence odds ratio will overestimate the prevalence risk ratio when it is greater than than 1 or understimate the prevalence risk ratio when it is less than 1.

Measures of effect in the exposed include the attributable risk (for cohort studies where the outcome of interest is expressed as an incidence risk), attributable rate (for cohort studies where the outcome of interest is expressed as an incidence rate) and prevalence risk (for cross-sectional studies where the outcome of interest is expressed as a prevalence risk). The attributable risk is the incidence risk of the outcome in the exposed minus the incidence risk of the outcome in the unexposed.

The attributable risk provides a measure of the absolute increase or decrease in outcome risk that is associated with exposure. The attributable fraction is the proportion of study outcomes in the exposed group that is attributable to exposure.

The number needed to treat (NNT) is the inverse of the attributable risk. Depending on the outcome of interest we use different labels for NNT. When dealing with an outcome that is desirable (e.g., treatment success) we call NNT the number needed to treat for benefit, NNTB. NNTB equals the number of subjects who would have to be exposed to result in a single (desirable) outcome. When dealing with an outcome that is undesirable (e.g., death) we call NNT the number needed to treat for harm, NNTH. NNTH equals the number of subjects who would have to be exposed to result in a single (undesirable) outcome.

Measures of effect in the population include the attributable risk in the population (for cohort studies where the outcome of interest is expressed as an incidence risk) and the attributable prevalence in the population (for cross-sectional studies where the outcome of interest is expressed as a prevalence risk). The population attributable risk provides a measure of the absolute increase or decrease in outcome risk in the population that is associated with exposure. The population attributable fraction is the proportion of study outcomes in the populaton that is attributable to exposure.

Point estimates and confidence intervals for the prevalence ratio and incidence risk ratio are calculated using the 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 for the odds ratio are calculated using the 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 Lash et al (2021) 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 because they are widely used and should 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 statistically significant.

The Mantel-Haenszel (Woolf) test of homogeneity of the odds ratio are based on Jewell (2004, p 152 - 158). Thanks to Jim Robison-Cox for sharing his implementation of these functions.

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Examples

```
## EXAMPLE 1:
## A cross sectional study investigating the relationship between habitual
## consumption of dry food and feline lower urinary tract disease (FLUTD) was
## conducted (Willeberg 1977). Counts of individuals in each group were as
## follows:

## Dry food exposed (cases, non-cases) 13, 2163
## Dry food unexposed (cases, non-cases) 5, 3349

## Outcome variable (FLUTD) as columns:
dat.v01 <- c(13,2163,5,3349); dat.v01

epi.2by2(dat = dat.v01, method = "cross.sectional", elab = "Dry food",
   olab = "FLUTD", digits = 2, conf.level = 0.95, units = 100,
   interpret = FALSE, outcome = "as.columns")

## Outcome variable (FLUTD) as rows:
dat.v01 <- c(13,5,2163,3349); dat.v01

epi.2by2(dat =  dat.v01, method = "cross.sectional", elab = "Dry food",
   olab = "FLUTD", digits = 2, conf.level = 0.95, units = 100,
   interpret = FALSE, outcome = "as.rows")

## The prevalence of FLUTD in dry food positive cats was 4.01 (95% CI 1.43 to
## 11.23) times the prevalence of FLUTD in dry food negative cats.

## In dry food positive cats, 75% (95% CI 33% to 91%) of FLUTD cases were
```

```
## attributable to feeding dry food.

## Fifty-four percent of FLUTD cases in the population was attributable
## to feeding dry food (95% CI 32% to 75%).

## An unmeasured confounder in this study would need to be associated with
## both dry food and FLUTD by a risk ratio of at least 7.48 (each) to
## completely account for the observed odds ratio of 4.03.


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

library(MASS)
dat.df02 <- birthwt; head(dat.df02)

## Generate a table of cell frequencies. First, set the outcome and exposure
## as factors and set their levels appropriately so the frequencies in the
## 2 by 2 table come out in the conventional format:
dat.df02$low <- factor(dat.df02$low, levels = c(1,0))
dat.df02$smoke <- factor(dat.df02$smoke, levels = c(1,0))
dat.df02$race <- factor(dat.df02$race, levels = c(1,2,3))
dat.tab02 <- table(dat.df02$smoke, dat.df02$low, dnn = c("Smoke", "Low BW"))
print(dat.tab02)

## Compute the odds ratio and other measures of association:
epi.2by2(dat = dat.tab02, method = "cohort.count", elab = "Smoke",
   olab = "Low BW", digits = 2, conf.level = 0.95, units = 100,
   interpret = FALSE, outcome = "as.columns")

## The odds of having a low birth weight child for smokers was 2.02
## (95% CI 1.08 to 3.78) times the odds of having a low birth weight child
## for non-smokers.

## An unmeasured confounder in this study would need to be associated with
## both smoking and low BW by a risk ratio of at least 2.60 (each) to
## completely account for the observed odds ratio of 2.02.

## Stratify by race:
dat.tab02 <- table(dat.df02$smoke, dat.df02$low, dat.df02$race,
   dnn = c("Smoke", "Low BW", "Race"))
print(dat.tab02)

## Compute the crude odds ratio, the Mantel-Haenszel adjusted odds ratio
## and other measures of association:
dat.epi02 <- epi.2by2(dat = dat.tab02, method = "cohort.count", elab = "Smoke",
   olab = "Low BW", digits = 2, conf.level = 0.95, units = 100,
   interpret = FALSE, outcome = "as.columns")
print(dat.epi02)

## The Mantel-Haenszel test of homogeneity of the strata odds ratios is not
## statistically significant (chi square test statistic 2.800; df 2;
```

```
## p-value = 0.25) so we accept the null hypothesis and conclude that the
## odds ratios for each strata of race are the same.

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

## After controlling for the confounding effect of race, a (residual)
## confounder in this study would need to be associated with
## both smoking and low BW by a risk ratio of at least 3.73 (each) to
## completely account for the observed Mantel-Haenszel adjusted odds ratio
## of 3.09.

## 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:

dat.epi02$massoc.detail$ARisk.mh.green
dat.epi02$massoc.detail$ARisk.mh.wald

## How many mothers need to stop smoking to avoid one low birth weight baby?
dat.epi02$massoc.interp$text[dat.epi02$massoc.interp$var ==
   "NNTB NNTH (crude)"]

## The crude incidence risk of low BW among those that were smoke positive was
## 15 (95% CI 1.6 to 29) per 100 population units greater than the crude
## incidence risk of low BW among those that were smoke negative. The number
## needed to expose to smoking to increase low BW frequency by one was 7
## (95% CI 3 to 62)."

dat.epi02$massoc.interp$text[dat.epi02$massoc.interp$var == "NNTB NNTH (M-H)"]

## The Mantel-Haenszel adjusted incidence risk of low BW among those that were
## smoke positive was 22 (95% CI 1.4 to 43) per 100 population units greater
## than the Mantel-Haenszel adjusted incidence risk of low BW among those that
## were smoke negative. The number needed to expose to smoke to increase low
## BW frequency by one was 5 (95% CI 2 to 71)."

## Now turn dat.tab02 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:
dat.df02 <- data.frame(dat.tab02); head(dat.df02)

## Re-format dat.df02 (a summary count data frame) into tabular format using
## the xtabs function:
dat.tab02 <- xtabs(Freq ~ Smoke + Low.BW + Race, data = dat.df02)
print(dat.tab02)

# dat02.tab can now be passed to epi.2by2:
dat.epi02 <- epi.2by2(dat = dat.tab02, method = "cohort.count", elab = "Smoke",
   olab = "Low BW", digits = 2, conf.level = 0.95, units = 100,
   interpret = FALSE, outcome = "as.columns")
print(dat.epi02)
```

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

## What are the Cornfield confidence limits, the maximum likelihood
## confidence limits and the score confidence limits for the crude
## incidence odds ratio?
dat.epi02$massoc.detail$OR.crude.cfield
dat.epi02$massoc.detail$OR.crude.mle
dat.epi02$massoc.detail$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 incidence odds ratios and compare them
## with the Mantel-Haenszel adjusted incidence odds ratio.

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

nstrata <- 1:dim(dat.tab02)[3]
strata.lab <- paste("Strata ", nstrata, sep = "")
y.at <- c(nstrata, max(nstrata) + 1)
y.lab <- c("M-H", strata.lab)
x.brk <- 2^seq(from = -2, to = 5, by = 1)

or.p <- c(dat.epi02$massoc.detail$OR.mh$est,
   dat.epi02$massoc.detail$OR.strata.cfield$est)
or.l <- c(dat.epi02$massoc.detail$OR.mh$lower,
   dat.epi02$massoc.detail$OR.strata.cfield$lower)
or.u <- c(dat.epi02$massoc.detail$OR.mh$upper,
   dat.epi02$massoc.detail$OR.strata.cfield$upper)
dat.df02 <- data.frame(y.at, y.lab, or.p, or.l, or.u)

ggplot(data = dat.df02, aes(x = or.p, y = y.at)) +
  theme_bw() +
  geom_point() +
  geom_errorbar(aes(xmin = or.l, xmax = or.u), width = 0.2, orientation = "y") +
  labs(x = "Odds ratio", y = "Strata") +
  scale_x_continuous(trans = log2_trans(), breaks = x.brk,
                     limits = range(x.brk)) +
  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:
## Same as Example 2 but showing how a 2 by 2 contingency table can be prepared
```

```
## using functions from the tidyverse package:

## Not run:
library(MASS); library(tidyverse)

dat.df03 <- birthwt; head(dat.df03)

dat.df03 <- dat.df03 %>%
  mutate(low = factor(low, levels = c(1,0), labels = c("yes","no"))) %>%
  mutate(smoke = factor(smoke, levels = c(1,0), labels = c("yes","no"))) %>%
  group_by(smoke, low) %>%
  summarise(n = n())
dat.df03

## View the data in conventional 2 by 2 table format:
pivot_wider(dat.df03, id_cols = c(smoke), names_from = low, values_from = n)

dat.epi03 <- epi.2by2(dat = dat.df03, method = "cohort.count", elab = NA,
   olab = NA, digits = 2, conf.level = 0.95, units = 100, interpret = FALSE,
   outcome = "as.columns")
dat.epi03

## End(Not run)

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

## Stratify by race:
## Not run:
library(MASS); library(tidyverse)

dat.df04 <- birthwt; head(dat.df04)

dat.df04 <- dat.df04 %>%
  mutate(low = factor(low, levels = c(1,0), labels = c("yes","no"))) %>%
  mutate(smoke = factor(smoke, levels = c(1,0), labels = c("yes","no"))) %>%
  mutate(race = factor(race)) %>%
  group_by(race, smoke, low) %>%
  summarise(n = n())
dat.df04

## View the data in conventional 2 by 2 table format:
pivot_wider(dat.df04, id_cols = c(race, smoke),
   names_from = low, values_from = n)

dat.epi04 <- epi.2by2(dat = dat.df04, method = "cohort.count", elab = NA,
   olab = NA, digits = 2, conf.level = 0.95, units = 100, interpret = FALSE,
   outcome = "as.columns")
dat.epi04

## End(Not run)
```

```
## The Mantel-Haenszel test of homogeneity of the strata odds ratios is not
## statistically significant (chi square test statistic 2.800; df 2;
## p-value = 0.25). We accept the null hypothesis and conclude that the
## incidence odds ratios for each strata of race are the same.

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


## EXAMPLE 4:
## Sometimes you'll have only event count data for a stratified analysis. This
## example shows how to coerce a three column matrix listing (in order) counts
## of outcome positive individuals, counts of outcome negative individuals (or
## total time at risk, as in the example below) and strata into a three
## dimensional array.

## We assume that two rows are recorded for each strata. The first for those
## exposed and the second for those unexposed. Note that the strata variable
## needs to be numeric (not a factor).

dat.m04 <- matrix(c(1308,884,200,190,4325264,13142619,1530342,5586741,1,1,2,2),
   nrow = 4, ncol = 3, byrow = FALSE)
colnames(dat.m04) <- c("obs","tar","grp")
dat.df04 <- data.frame(dat.m04)

## Here we use the apply function to coerce the two rows for each strata into
## tabular format. An array is created of with the length of the third
## dimension of the array equal to the number of strata:
dat.tab04 <- sapply(1:length(unique(dat.df04$grp)), function(x)
   as.matrix(dat.df04[dat.df04$grp == x,1:2], ncol = 2, byrow = TRUE),
   simplify = "array")
dat.tab04

epi.2by2(dat = dat.tab04, method = "cohort.time", elab = NA,
   olab = NA, digits = 2, conf.level = 0.95, units = 1000 * 365.25,
   interpret = FALSE, outcome = "as.columns")

## The Mantel-Haenszel adjusted incidence rate ratio was 4.39 (95% CI 4.06
## to 4.75).


## EXAMPLE 5:
## 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.

dat.v05 <- c(136,22050,1709,127650)

dat.epi05 <- epi.2by2(dat = dat.v05, method = "cohort.time",
   elab = "Vis impaired", olab = "Cancer", digits = 2,
```

```
   conf.level = 0.95, units = 1000, interpret = FALSE, outcome = "as.columns")
summary(dat.epi05)$massoc.detail$ARate.strata.wald

## The incidence rate of cancer was 7.22 (95% CI 6.00 to 8.43) cases per
## 1000 person-years less in the blind, compared with those who were not
## blind but had severe visual impairment.

round(summary(dat.epi05)$massoc.detail$IRR.strata.wald, digits = 2)

## The incidence rate of cancer in the blind group was less than half that
## of the comparison group (incidence rate ratio 0.46, 95% CI 0.38 to 0.55).


## EXAMPLE 6:
## 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 vectors ai,
## bi, ci and di list (for each herd) the number of cows in the E+R+, E+R-,
## E-R+ and E-R- groups, where `E' denotes exposure and `R' denotes recovery:

## 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.df06 <- data.frame(hid, ai, bi, ci, di)
head(dat.df06)

## Re-format data 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.df06 <- data.frame(hid, exp, out, n = c(ai,bi,ci,di))
dat.tab06 <- xtabs(n ~ exp + out + hid, data = dat.df06)
print(dat.tab06)

epi.2by2(dat = dat.tab06, method = "cohort.count",
   elab = "Treat", olab = "Recovery", digits = 2,
   conf.level = 0.95, units = 100, interpret = FALSE, outcome = "as.columns")

## The Mantel-Haenszel test of homogeneity of the strata incidence odds ratios
## is not statistically significant (chi square test statistic 5.276; df 7;
## p-value = 0.63). We accept the null hypothesis and conclude that the
## incidence odds ratios for each strata of herd are the same.

## The Mantel-Haenszel adjusted incidence risk of recovery among those that
## were treat positive was 1.94 (95
## Haenszel adjusted incidence risk of recovery among those that were
## treat negative.

## End(Not run)
```

epi.about *The library epiR: summary information*

Description

Tools for the analysis of epidemiological data.

Usage

```
epi.about()
```

Details

More information about the epiR package can be found at https://mvs.unimelb.edu.au/research/groups/veterinary- and https://www.ausvet.com.au/.

FREQUENTLY ASKED QUESTIONS

I have some diagnostic test results. How do I work out the expected number of true positive and false positive results? See epi.fpos: Compute the number of true positives, false positives, true negatives and false negatives given the number of individuals tested, the design prevalence and diagnostic test sensitivity and specificity.

How do I work out a sample size to estimate the prevalence of disease? If simple random sampling has been used see epi.sssimpleestb. If two-stage cluster design sampling has been used see epi.ssclus2estb.

How do I work out diagnostic test sensitivity and specificity from a set of test results? See epi.tests.

How do I work out the true prevalence of disease based on results from an imperfect diagnostic test? See epi.prev.

How do I calculate an odds ratio and incidence risk ratio on the basis of data presented in a 2 times 2 table? See epi.2by2.

How do I calculate a confidence interval for an incidence risk estimate? See epi.conf.

I've collected samples from a population and have tested them — all returning a negative result. What is the maximum prevalence of disease in this population if disease is actually present? See rsu.pstar.

I've collected samples from a population and have tested them — all returning a negative result. What is the probability that the prevalence of disease is less than or equal to a specified design prevalence? See rsu.sep.

How do I calculate the standardised mortality ratio for a single study area? See the epi.smr function. Example 1 in epi.bohning shows you how to calculate an expected value. To calculate SMRs and their confidence intervals for a series of study areas (instead of one) see the epi.conf function using ctype = "smr".

FUNCTIONS AND DATASETS

The following is a summary of the main functions and datasets in the **epiR** package. An alphabetical list of all functions and datasets is available by typing `library(help = epiR)`.

For further information on any of these functions, type `help(name)` or `?name` where `name` is the name of the function or dataset.

For details on how to use **epiR** for routine epidemiological work start R, type `help.start()` to open the help browser and navigate to `Packages` > `epiR` > `Vignettes`.

CONTENTS:

The functions in **epiR** can be categorised into two main groups: tools for epidemiological analysis and tools for the analysis of surveillance data. A summary of the package functions is as follows:

I. EPIDEMIOLOGY

1. Descriptive statistics:

`epi.conf`	Confidence intervals.
`epi.descriptives`	Descriptive statistics.

2. Measures of health and measures of association:

`epi.2by2`	Measures of association from data presented in a 2 by 2 table.
`epi.directadj`	Directly adjusted incidence rate estimates.
`epi.edr`	Compute estimated dissemination ratios from outbreak event data.
`epi.empbayes`	Empirical Bayes estimates of observed event counts.
`epi.evalue`	Compute E-value for risk, rate, odds and hazard ratio estimates.
`epi.indirectadj`	Indirectly adjusted incidence risk estimates.
`epi.insthaz`	Instantaneous hazard estimates based on Kaplan-Meier survival estimates.
`epi.smr`	Confidence intervals and tests of statistical significance of the standardised mortality [morbidity] ratio.

3. Diagnostic tests:

`epi.betabuster`	An R version of Wes Johnson and Chun-Lung Su's Betabuster.
`epi.blcm.paras`	Number of parameters to be inferred and number of informative priors for a BLCA.
`epi.fpos`	Calculate the expected number of false positive and false negative test results.
`epi.herdtest`	Estimate the characteristics of diagnostic tests applied at the herd (group) level.
`epi.iref`	Calculate diagnostic sensitivity and specificity using an imperfect reference test.
`epi.nomogram`	Compute the post-test probability of disease given characteristics of a diagnostic test.
`epi.pooled`	Estimate herd test characteristics when samples are pooled.
`epi.prev`	Compute the true prevalence of a disease in a population on the basis of an imperfect test.
`epi.tests`	Sensitivity, specificity and predictive value of a diagnostic test.

4. Meta-analysis:

epi.dsl	Mixed-effects meta-analysis of binary outcome data using the DerSimonian and Laird method.
epi.iv	Fixed-effects meta-analysis of binary outcome data using the inverse variance method.
epi.mh	Fixed-effects meta-analysis of binary outcome data using the Mantel-Haenszel method.
epi.smd	Fixed-effects meta-analysis of continuous outcome data using the standardised mean difference method.

5. Regression analysis tools:

epi.cp	Extract unique covariate patterns from a data set.
epi.cpresids	Compute covariate pattern residuals from a logistic regression model.
epi.interaction	Relative excess risk due to interaction in a case-control study.

6. Data manipulation tools:

epi.asc	Write matrix to an ASCII raster file.
epi.convgrid	Convert British National Grid georeferences to easting and northing coordinates.
epi.dms	Convert decimal degrees to degrees, minutes and seconds and vice versa.
epi.ltd	Calculate lactation to date and standard lactation (that is, 305 or 270 day) milk yields.
epi.offset	Create an offset vector based on a list suitable for WinBUGS.
epi.RtoBUGS	Write data from an R list to a text file in WinBUGS-compatible format.

7. Sample size calculations:

The naming convention for the sample size functions in **epiR** is: `epi.ss` (sample size) + an abbreviation to represent the sampling design (e.g., `simple`, `strata`, `clus1`, `clus2`) + an abbreviation of the objectives of the study (`est` when you want to estimate a population parameter or `comp` when you want to compare two groups) + a single letter defining the outcome variable type (`b` for binary, `c` for continuous and `s` for survival data).

epi.sssimpleestb	Sample size to estimate a binary outcome using simple random sampling.
epi.sssimpleestc	Sample size to estimate a continuous outcome using simple random sampling.
epi.ssstrataestb	Sample size to estimate a binary outcome using stratified random sampling.
epi.ssstrataestc	Sample size to estimate a continuous outcome using stratified random sampling.
epi.ssclus1estb	Sample size to estimate a binary outcome using one-stage cluster sampling.
epi.ssclus1estc	Sample size to estimate a continuous outcome using one-stage cluster sampling.
epi.ssclus2estb	Sample size to estimate a binary outcome using two-stage cluster sampling.
epi.ssclus2estc	Sample size to estimate a continuous outcome using two-stage cluster sampling.
epi.ssxsectn	Sample size, power or detectable prevalence ratio for a cross-sectional study.
epi.sscohortc	Sample size, power or detectable risk ratio for a cohort study using count data.
epi.sscohortt	Sample size, power or detectable risk ratio for a cohort study using time at risk data.
epi.sscc	Sample size, power or detectable odds ratio for case-control studies.
epi.sscompb	Sample size, power and detectable risk ratio when comparing binary outcomes.
epi.sscompc	Sample size, power and detectable risk ratio when comparing continuous outcomes.

epi.sscomps	Sample size, power and detectable hazard when comparing time to event.
epi.ssequb	Sample size for a parallel equivalence or equality trial, binary outcome.
epi.ssequc	Sample size for a parallel equivalence or equality trial, continuous outcome.
epi.sssupb	Sample size for a parallel superiority trial, binary outcome.
epi.sssupc	Sample size for a parallel superiority trial, continuous outcome.
epi.ssninfb	Sample size for a non-inferiority trial, binary outcome.
epi.ssninfc	Sample size for a non-inferiority trial, continuous outcome.
epi.ssdetect	Sample size to detect an event.
epi.ssdxsesp	Sample size to estimate the sensitivity or specificity of a diagnostic test.
epi.ssdxtest	Sample size to validate a diagnostic test in the absence of a gold standard.

8. Miscellaneous functions:

epi.prcc	Compute partial rank correlation coefficients.
epi.psi	Compute proportional similarity indices.
epi.realrisk	Return absolute risks from odds, incidence risk and hazard ratios.
epi.mbf	Return Minimum Bayes Factor using the Goodman or Sellke et al. method.

9. Data sets:

epi.epidural	Rates of use of epidural anaesthesia in trials of caregiver support.
epi.incin	Laryngeal and lung cancer cases in Lancashire 1974 - 1983.
epi.SClip	Lip cancer in Scotland 1975 - 1980.

II. SURVEILLANCE

Below, SSe stands for surveillance system sensitivity. That is, the average probability that a surveillance system (as a whole) will return a positive surveillance outcome, given disease is present in the population at a level equal to or greater than a specified design prevalence.

1. Representative sampling — sample size:

rsu.sspfree.rs	Defined probability of disease freedom.
rsu.sssep.rs	SSe, perfect test specificity.
rsu.sssep.rs2st	SSe, two stage sampling.
rsu.sssep.rsfreecalc	SSe, imperfect test specificity.
rsu.sssep.rspool	SSe, pooled sampling.

2. Representative sampling — surveillance system sensitivity and specificity:

rsu.sep.rs	SSe, representative sampling.

rsu.sep.rs2st	SSe, representative two-stage sampling.
rsu.sep.rsmult	SSe, representative multiple surveillance components.
rsu.sep.rsfreecalc	SSe, imperfect test specificity.
rsu.sep.rspool	SSe, representative pooled sampling.
rsu.sep.rsvarse	SSe, varying surveillance unit sensitivity.
rsu.spp.rs	Surveillance system specificity.

3. Representative sampling — probability of disease freedom:

rsu.pfree.rs	Probability of disease freedom for a single or multiple time periods.
rsu.pfree.equ	Equilibrium probability of disease freedom.

4. Risk-based sampling — sample size:

rsu.sssep.rbsrg	SSe, single sensitivity for each risk group.
rsu.sssep.rbmrg	SSe, multiple sensitivities within risk groups.
rsu.sssep.rb2st1rf	SSe, 2 stage sampling, 1 risk factor.
rsu.sssep.rb2st2rf	SSe, 2 stage sampling, 2 risk factors.

5. Risk-based sampling — surveillance system sensitivity and specificity:

rsu.sep.rb	SSe, risk-based sampling.
rsu.sep.rb1rf	SSe, risk-based sampling, 1 risk factor.
rsu.sep.rb2rf	SSe, risk-based sampling, 2 risk factors.
rsu.sep.rbvarse	SSe, risk-based sampling, varying unit sensitivity.
rsu.sep.rb2st	SSe, 2-stage risk-based sampling.

6. Risk-based sampling — probability of disease freedom:

rsu.pfree.equ	Equilibrium probability of disease freedom.

7. Census sampling — surveillance system sensitivity:

rsu.sep.cens	SSe, census sampling.

8. Passive surveillance — surveillance system sensitivity:

rsu.sep.pass	SSe, passive surveillance.

9. Miscellaneous functions:

rsu.adjrisk	Adjusted risk values.
rsu.dxtest	Series and parallel diagnostic test interpretation.

rsu.epinf	Effective probability of disease.
rsu.pstar	Design prevalence back calculation.
rsu.sep	Probability disease is less than specified design prevalence.

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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 `NA`s 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, imsure, 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`.
`imsure`	a character string, if `"greater than"` you are making the statement that you are `conf` confident that the true value of the variable of interest is greater than `x`. If `"less than"` 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 version of BetaBuster. If r equals the number of times an event has occurred after n trials, shape1 = (r + 1) and shape2 = (n - r + 1).

Take care when you're parameterising probability estimates that are at the extremes of the 0 to 1 bounds. If the returned shape1 parameter is equal to the value of max.shape1 (which, by default is 100) consider increasing the value of the max.shape1 argument. The epi.betabuster functions issues a warning if these conditions are met.

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.
exp	a statement of the arguments used for this instance of the function.

Author(s)

Simon Firestone (Melbourne Veterinary School, Faculty of Science, The University of Melbourne, Parkville Victoria 3010, 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.

Su C-L, Johnson W (2014) Beta Buster. Software for obtaining parameters for the Beta distribution based on expert elicitation. URL: https://cadms.vetmed.ucdavis.edu/diagnostic/software.

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.beta01 <- epi.betabuster(mode = 0.90, conf = 0.80, imsure = "greater than",
   x = 0.75, conf.level = 0.95, max.shape1 = 100, step = 0.001)
rval.beta01$shape1; rval.beta01$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.beta01$shape1 - 1; r

## from 10 trials, n:
n <- rval.beta01$shape2 + rval.beta01$shape1 - 2; n

dat.df01 <- data.frame(x = seq(from = 0, to = 1, by = 0.001),
   y = dbeta(x = seq(from = 0, to = 1,by = 0.001),
   shape1 = rval.beta01$shape1, shape2 = rval.beta01$shape2))

## Density plot of the estimated beta distribution:

## Not run:
library(ggplot2)

ggplot(data = dat.df01, aes(x = x, y = y)) +
  theme_bw() +
  geom_line() +
  scale_x_continuous(name = "Test sensitivity") +
  scale_y_continuous(name = "Density")

## End(Not run)


## EXAMPLE 2:
## The most likely value of the specificity of a PCR for coxiellosis in
## small ruminants is 1.00 and we're 97.5% certain that this estimate is
## greater than 0.99. What are the shape1 and shape2 parameters for a beta
## distribution satisfying these constraints?

epi.betabuster(mode = 1.00, conf = 0.975, imsure = "greater than", x = 0.99,
   conf.level = 0.95, max.shape1 = 100, step = 0.001)

## The shape1 and shape2 parameters for the beta distribution that satisfy the
## constraints listed above are 100 and 1, respectively. epi.betabuster
## issues a warning that the value of shape1 equals max.shape1. Increase
```

```
## max.shape1 to 500:

epi.betabuster(mode = 1.00, conf = 0.975, imsure = "greater than", x = 0.99,
   conf.level = 0.95, max.shape1 = 500, step = 0.001)

## The shape1 and shape2 parameters for the beta distribution that satisfy the
## constraints listed above are 367.04 and 1, respectively.
```

`epi.blcm.paras` *Number of parameters to be inferred and number of informative priors required for a Bayesian latent class model*

Description

Returns the number of unknown parameters to be inferred and the number of informative priors likely to be needed for an identifiable Bayesian latent class model to estimate diagnostic sensitivity and specificity in the absence of a gold standard.

Usage

```
epi.blcm.paras(ntest.dep = 2, ntest.indep = 1, npop = 2)
```

Arguments

`ntest.dep`	scalar, the number of conditionally dependent tests evaluated.
`ntest.indep`	scalar, the number of conditionally independent tests evaluated.
`npop`	scalar, the number of populations with a distinct prevalence investigated.

Value

A list containing the following:

`df`	scalar, the degrees of freedom in the available data.
`npars`	scalar, the number of unknown parameters to be inferred.
`ninf.priors`	scalar, the number of informative priors likely to be needed for an identifiable model.

Note

A model may still be useful for inference if it has less informative priors, though cautious interpretation is warranted, typically with a sensitivity analysis of the influence of the priors on the findings.

Author(s)

Simon Firestone and Allison Cheung (Melbourne Veterinary School, Faculty of Science, The University of Melbourne, Parkville Victoria, Australia), Nagendra Singanallur (Australian Centre for Disease Preparedness, Newcomb Victoria, Australia).

Examples

```
## EXAMPLE 1 --- Two conditionally dependent tests, 1 population:
epi.blcm.paras(ntest.dep = 2, ntest.indep = 0, npop = 1)

## This model has 3 degrees of freedom. The model has 7 unknown parameters to
## be inferred. At least 4 informative priors are required.


## EXAMPLE 2 --- Two conditionally dependent tests, 2 populations:
epi.blcm.paras(ntest.dep = 2, ntest.indep = 0, npop = 2)

## This model has 6 degrees of freedom. The model has 8 unknown parameters to
## be inferred. At least 2 informative priors are required.


## EXAMPLE 3 --- Two conditionally dependent tests, 3 populations:
epi.blcm.paras(ntest.dep = 2, ntest.indep = 0, npop = 3)

## This model has 9 degrees of freedom. The model has 9 unknown parameters to
## be inferred. This model may be able to proceed without informative priors.


## EXAMPLE 4 --- Two conditionally dependent tests, 1 independent test, 1
## population:
epi.blcm.paras(ntest.dep = 2, ntest.indep = 1, npop = 1)

## This model has 7 degrees of freedom. The model has 9 unknown parameters to
## be inferred. At least 2 informative priors are required.


## EXAMPLE 5 --- Two conditionally dependent tests, 1 independent test, 2
## populations:
epi.blcm.paras(ntest.dep = 2, ntest.indep = 1, npop = 2)

## This model has 14 degrees of freedom. The model has 10 unknown parameters to
## be inferred. This model may be able to proceed without informative priors.


## EXAMPLE 6 --- Three conditionally dependent tests, 1 population:
epi.blcm.paras(ntest.dep = 3, ntest.indep = 0, npop = 1)

## This model has 7 degrees of freedom. The model has 13 unknown parameters to
## be inferred. At least 6 informative priors are required.


## EXAMPLE 7 --- Three conditionally dependent tests, 2 populations:
epi.blcm.paras(ntest.dep = 3, ntest.indep = 0, npop = 2)

## This model has 14 degrees of freedom. The model has 14 unknown parameters to
## be inferred. This model may be able to proceed without informative priors.
```

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 listing: 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

```
## EXAMPLE 1:
## Lip cancer in Scotland, 1975 to 1980:
data(epi.SClip)
obs <- epi.SClip$cases
pop <- epi.SClip$population

## Calculate the expected number of lip cancer cases per district:
exp <- (sum(obs) / sum(pop)) * pop

## Bohning's test:
epi.bohning(obs, exp, alpha = 0.05)

## The test statistic was 53.33. The associated P value was <0.01. We reject
## the null hypothesis of no over dispersion and accept the null hypothesis
## concluding that the lip cancer data are over dispersed.
```

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.

Rashid M, Stevenson M, Waenga S, Mirams G, Campbell A, Vaughan J, Jabbar A (2018). Comparison of McMaster and FECPAK methods for counting nematode eggs in the faeces of alpacas. Parasites & Vectors 11, 278. DOI: 10.1186/s13071-018-2861-1.

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

dat.df01 <- data.frame(method1, method2)
rval.ccc01 <- epi.ccc(method1, method2, ci = "z-transform", conf.level = 0.95,
   rep.measure = FALSE)

rval.lab01 <- data.frame(lab = paste("CCC: ",
   round(rval.ccc01$rho.c[,1], digits = 2), " (95% CI ",
   round(rval.ccc01$rho.c[,2], digits = 2), " - ",
   round(rval.ccc01$rho.c[,3], digits = 2), ")", sep = ""))

z <- lm(method2 ~ method1)
alpha <- summary(z)$coefficients[1,1]
beta <-  summary(z)$coefficients[2,1]
rval.lm01 <- data.frame(alpha, beta)

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

ggplot(data = dat.df01, aes(x = method1, y = method2)) +
  theme_bw() +
  geom_point() +
  geom_abline(intercept = 0, slope = 1) +
  geom_abline(data = rval.lm01, aes(intercept = alpha, slope = beta),
     linetype = "dashed") +
  scale_x_continuous(limits = c(0,3), name = "Method 1") +
  scale_y_continuous(limits = c(0,3), name = "Method 2") +
  geom_text(data = rval.lab01, x = 0.5, y = 2.95, label = rval.lab01$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)
```

```
rval.ccc02 <- epi.ccc(x, y, ci = "z-transform", conf.level = 0.95,
   rep.measure = FALSE)
rval.df02 <- data.frame(mean = rval.ccc02$blalt[,1],
   delta = rval.ccc02$blalt[,2])

## Not run:
library(ggplot2)

ggplot(data = rval.ccc02$blalt, aes(x = mean, y = delta)) +
  theme_bw() +
  geom_point() +
  geom_hline(data = rval.ccc02$sblalt, aes(yintercept = lower), linetype = 2) +
  geom_hline(data = rval.ccc02$sblalt, aes(yintercept = upper), linetype = 2) +
  geom_hline(data = rval.ccc02$sblalt, aes(yintercept = est), linetype = 1) +
  scale_x_continuous(limits = c(0,800),
     name = "Average PEFR by two meters (L/min)") +
  scale_y_continuous(limits = c(-150,150),
     name = "Difference in PEFR (L/min)")

## End(Not run)


## EXAMPLE 3:
## Setting limits of agreement when your data are skewed. See Euser et al.
## (2008) for details and Rashid et al. (2018) for an applied example.
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)

rval.ccc03 <- epi.ccc(x, y, ci = "z-transform",
   conf.level = 0.95, rep.measure = FALSE)

## Not run:
library(ggplot2)

ggplot(data = rval.ccc03$blalt, aes(x = mean, y = delta)) +
  theme_bw() +
  geom_point() +
  geom_hline(data = rval.ccc03$sblalt, aes(yintercept = lower), linetype = 2) +
  geom_hline(data = rval.ccc03$sblalt, aes(yintercept = upper), linetype = 2) +
  geom_hline(data = rval.ccc03$sblalt, aes(yintercept = est), linetype = 1) +
  scale_x_continuous(limits = c(0,8000),
     name = "Average of the two measurements") +
  scale_y_continuous(limits = c(-8000,8000),
     name = "Difference in the two measurements")

## 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.ccc03 <- 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.ccc03$sblalt$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(

data = rval.ccc03$blalt, aes(x = mean, y = delta)) +
  theme_bw() +
  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) +
  scale_x_continuous(limits = c(0,8000),
     name = "Average of the two measurements") +
  scale_y_continuous(limits = c(-8000,8000),
     name = "Difference in the two measurements")

## End(Not run)
```

---

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, fleiss, agresti, clopper-pearson and jeffreys. 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 events, the second column specifies the population size.

The methodology implemented here follows Altman, Machin, Bryant, and Gardner (2000). Where method is inc.risk or prevalence 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 (2012)
inc.risk, fleiss	Fleiss (1981)
inc.risk, agresti	Agresti and Coull (1998)
inc.risk, clopper-pearson	Clopper and Pearson (1934)
inc.risk, jeffreys	Brown et al. (2001)
prevalence, exact	Collett (1999)
prevalence, wilson	Wilson (1927)
prevalence, fleiss	Fleiss (1981)
prevalence, agresti	Agresti and Coull (1998)
prevalence, clopper-pearson	Clopper and Pearson (1934)
prevalence, jeffreys	Brown et al. (2001)
inc.rate, exact	Ulm (1990)
inc.rate, byar	Rothman (2012)
odds	Ederer and Mantel (1974)
ratio	Ederer and Mantel (1974)
smr	Dobson et al. (1991)

The Wald interval often has inadequate coverage, particularly for small sample sizes and proportion estimates close to 0 or 1. Conversely, the Clopper-Pearson Exact method is conservative and tends to produce wider intervals than necessary. Brown et al. recommends the Wilson or Jeffreys methods when sample sizes are small and Agresti-Coull, Wilson, or Jeffreys methods for larger sample sizes.

The Clopper-Pearson interval is an early and very common method for calculating binomial confidence intervals. The Clopper-Pearson interval is sometimes called an 'exact' method because it is based on the cumulative probabilities of the binomial distribution (i.e., exactly the correct distribution rather than an approximation).

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 made on those prevalence and incidence risk methods that return a standard error (i.e., `method = "wilson"` or `method = "fleiss"`).

References

Agresti A, Coull B (1998). Approximate is better than 'exact' for interval estimation of binomial proportions. The American Statistician 52. DOI: 10.2307/2685469.

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.

Brown L, Cai T, Dasgupta A (2001). Interval estimation for a binomial proportion. Statistical Science 16: 101 - 133.

Clopper C, Pearson E (1934) The use of confidence or fiducial limits illustrated in the case of the binomial. Biometrika 26: 404 - 413. DOI: 10.1093/biomet/26.4.404.

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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 (2012). Epidemiology An Introduction. Oxford University Press, London, pp. 164 - 175.

Ulm K (1990). A simple method to calculate the confidence interval of a standardized mortality ratio. American Journal of Epidemiology 131: 373 - 375.

Wilson EB (1927) Probable inference, the law of succession, and statistical inference. Journal of the American Statistical Association 22: 209 - 212.

Examples

```
## EXAMPLE 1:
dat.v01 <- rnorm(n = 100, mean = 0, sd = 1)
epi.conf(dat = dat.v01, 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.df02 <- data.frame(group = group, val = val)
epi.conf(dat = dat.df02, 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.df03 <- data.frame(before, after)
epi.conf(dat = dat.df03, 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.m04 <- as.matrix(cbind(pos, neg))
round(epi.conf(dat = dat.m04, 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.m05 <- as.matrix(cbind(grp1, grp2))
round(epi.conf(dat = dat.m05, 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.m06 <- as.matrix(cbind(14,5,0,22))
round(epi.conf(dat = dat.m06, 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.m07 <- as.matrix(cbind(pos, pop))
epi.conf(dat = dat.m07, ctype = "prevalence", method = "exact", N = 1000,
   design = 1, conf.level = 0.95) * 100

## The estimated prevalence of brucellosis in this herd is 2.0 (95% CI 0.54 to
## 5.0) cases per 100 cattle at risk.


## 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.m08 <- as.matrix(cbind(obs, pop))
round(epi.conf(dat = dat.m08, 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 intracluster 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; D

## The design effect is 12.6. Now calculate the proportion protected. We set
## N to large number.
```

```
dat.m09 <- as.matrix(cbind(5898, 10363))
epi.conf(dat = dat.m09, 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 to 0.60). Recalculate this estimate assuming the data were from a
## simple random sample (i.e., where the design effect is one):

epi.conf(dat = dat.m09, ctype = "prevalence", method = "fleiss", N = 1000000,
   design = 1, conf.level = 0.95)

## If we had mistakenly assumed that data were a simple random sample the
## confidence interval for the proportion of birds protect 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 Brtish National Grid (EPSG 27700) easting and northing coordinates.

Usage

```
epi.convgrid(osref)
```

Arguments

`osref`	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

```
## EXAMPLE 1:
os.ref <- c("SJ505585","SJ488573","SJ652636")
epi.convgrid(os.ref)

os.ref <- c("SJ505585","SJ488573","ZZ123456")
epi.convgrid(os.ref)
```

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

Description

Extract the set of unique patterns from a set of covariates (explanatory variables).

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 allows for 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

```
## EXAMPLE 1:

## 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.df01 <- data.frame(obs, v1, v2)

dat.glm01 <- glm(obs ~ v1 + v2, family = binomial, data = dat.df01)
dat.mf01 <- model.frame(dat.glm01)

## Covariate pattern. Drop the first column of dat.mf01 (since column 1 is the
## outcome variable:
epi.cp(dat.mf01[,2:3])

## 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

```
## EXAMPLE 1:
dat.glm01 <- glm(case ~ spontaneous + induced, family = binomial(),
   data = infert)

## Covariate patterns:
dat.mf01 <- model.frame(dat.glm01)
dat.cp01 <- epi.cp(dat.mf01[-1])

dat.obs01 <- as.vector(by(infert$case, as.factor(dat.cp01$id),
   FUN = sum))
dat.fit01 <- as.vector(by(fitted(dat.glm01), as.factor(dat.cp01$id),
   FUN = min))
dat.cpr01 <- epi.cpresids(obs = dat.obs01, fit = dat.fit01,
   covpattern = dat.cp01)
head(dat.cpr01)
```

---

epi.descriptives *Descriptive statistics*

Description

Computes descriptive statistics for a numeric vector or a table of frequencies for a factor.

Usage

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

Arguments

dat	either a numeric vector or a factor.
conf.level	magnitude of the returned confidence intervals. Must be a single number between 0 and 1.

Value

If dat is numeric 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.

If dat is a factor a data frame listing:

level	The levels of the factor
n	The frequency of the respective factor level, including the column totals.

Examples

```
## EXAMPLE 1:
## Generate some data:
id <- 1:100
n <- rnorm(100, mean = 0, sd = 1)
dat.df01 <- data.frame(id, n)

# Add missing values:
missing <- dat.df01$id %in% sample(dat.df01$id, size = 20)
dat.df01$n[missing] <- NA

epi.descriptives(dat.df01$n, conf.level = 0.95)


## EXAMPLE 2:
## Generate some data:
n <- 1000; p.exp <- 0.50; p.dis <- 0.75
strata <- c(rep("A", times = n / 2), rep("B", times = n / 2))
exp <- rbinom(n = n, size = 1, prob = p.exp)
dis <- rbinom(n = n, size = 1, prob = p.dis)
dat.df02 <- data.frame(strata, exp, dis)

dat.df02$strata <- factor(dat.df02$strata)
dat.df02$exp <- factor(dat.df02$exp, levels = c("1", "0"))
head(dat.df02)

epi.descriptives(dat.df02$exp, conf.level = 0.95)
```

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 Australia, November 2000.

Examples

```
## EXAMPLE 1:
## 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 estimate of the precision of the heterogeneity term would be:

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

## The estimate of the precision of the heterogeneity term (tau) is 3.37.
## This can be re-expressed using the 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 is 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(x = z, y = fz, type = "l", ylab = "Probability density of tau")
```

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

Description

Compute directly adjusted incidence rate estimates.

Usage

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

Arguments

`obs`	a matrix providing counts of the observed number of events. Rows represent strata (e.g., region); columns represent the different levels of the variable to be adjusted for (e.g., age class) — the covariate. The sum of each row will equal the total number of observed events for each stratum. The row names of matrix `obs` are the appropriate strata names. The column names of `obs` are the appropriate level identifiers for the adjustment covariate. See the examples, below.
`tar`	a matrix representing population time at risk. Rows represent strata (e.g., region); columns represent the different levels of the variable to be adjusted for (e.g., age class) — the covariate. The sum of each row will equal the total population time at risk for each stratum. The row names of matrix `pop` must be the same as the row names used for matrix `obs`. The column names of matrix `pop` must be the same as the column names used for matrix `pop`. See the examples, below.
`std`	a matrix representing the standard population size for the different levels of the covariate to be adjusted for. The column names of matrix `std` must be the same as the column names used for matrices `obs` and `pop`.
`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.

Haneuse S, Rothman KJ. Stratification and Standardization. In: Lash TL, VanderWeele TJ, Haneuse S, Rothman KJ (2021). Modern Epidemiology. Lippincott - Raven Philadelphia, USA, pp. 415 - 445.

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. Data frame dat.df lists counts
## of leptospirosis cases and the number of dog years at risk for male and
## female dogs. In this example we stratify the data by city and the covariate
## is gender (with levels male and female). The data are presented as a matrix
## with two rows and two columns with city (Edinburgh, Glasgow) as the row
## names and levels of gender (male, female) as column names:

dat.df01 <- 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"))
```

```
obs01 <- matrix(dat.df01$obs, nrow = 2, byrow = TRUE,
   dimnames = list(c("ED","GL"), c("M","F")))
tar01 <- matrix(dat.df01$tar, nrow = 2, byrow = TRUE,
   dimnames = list(c("ED","GL"), c("M","F")))

## Create a standard population with equal numbers of male and female dogs:

std01 <- matrix(data = c(250,250), nrow = 1, byrow = TRUE,
   dimnames = list("", c("M","F")))

## Directly adjusted incidence rates:
epi.directadj(obs01, tar01, std01, units = 1, conf.level = 0.95)

## $crude
##  strata cov obs tar       est     lower     upper
##      ED   M  15  48 0.3125000 0.1749039 0.5154212
##      GL   M  53 180 0.2944444 0.2205591 0.3851406
##      ED   F  46 212 0.2169811 0.1588575 0.2894224
##      GL   F  16  71 0.2253521 0.1288082 0.3659577

## $crude.strata
##  strata obs tar       est     lower     upper
##      ED  61 260 0.2346154 0.1794622 0.3013733
##      GL  69 251 0.2749004 0.2138889 0.3479040

## $adj.strata
##  strata obs tar       est     lower     upper
##      ED  61 260 0.2647406 0.1866047 0.3692766
##      GL  69 251 0.2598983 0.1964162 0.3406224

## The adjusted incidence rate of leptospirosis in Glasgow dogs is 26 (95%
## CI 20 to 34) cases per 100 dog-years at risk. The confounding effect of
## gender has been removed by the adjusted incidence rate estimates.


## EXAMPLE 2:
## Here we provide a more flexible approach for calculating
## adjusted incidence rate estimates using Poisson regression. See Frome and
## Checkoway (1985) for details.

dat.glm02 <- glm(obs ~ city, offset = log(tar), family = poisson,
   data = dat.df01)
summary(dat.glm02)

## 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.pred02 <- predict(object = dat.glm02, 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.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(x = data.frame(est, lower, upper), digits = 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.


## EXAMPLE 3:
## Now adjust for the effect of gender and city and report the adjusted
## incidence rate estimates for each city:

dat.glm03 <- glm(obs ~ city + sex, offset = log(tar),
   family = poisson, data = dat.df01)
dat.pred03 <- predict(object = dat.glm03, 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.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(x = data.frame(est, lower, upper), digits = 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 4 --- 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.df01$pop <- dat.df01$tar

dat.glm04 <- glm(cbind(obs, pop - obs) ~ city + sex,
   family = "binomial", data = dat.df01)
dat.pred04 <- predict(object = dat.glm04, 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.glm04$family$linkinv(dat.pred04$fit)
lower <- dat.glm04$family$linkinv(dat.pred04$fit -
   (critval * dat.pred04$se.fit))
upper <- dat.glm04$family$linkinv(dat.pred04$fit +
   (critval * dat.pred04$se.fit))
round(x = data.frame(est, lower, upper), digits = 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.m01 <- matrix(c(41,38,7.836,-40,40,27.921),
```

```
   byrow = TRUE, nrow = 2)
epi.dms(dat.m01)


## EXAMPLE 2:
## Decimal degrees to degrees, minutes, seconds:
dat.m02 <- matrix(c(41.63551,-40.67442), nrow = 2)
epi.dms(dat.m02)
```

`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

```
## EXAMPLE 1:
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 ratios on the basis of a vector of count data (usually incident disease 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 outbreaks the *n*-day estimated dissemination ratio (EDR) at day *i* equals the total number of incident disease cases between day `i` and day `[i - (n - 1)]` (inclusive) divided by the total number of incident disease cases between day `(i - n)` and day `(i - 2n) + 1` (inclusive). EDR values are often calculated for each day of an outbreak and presented as a time series analysis. If the EDR is consistently less than one, the epidemic is said to be 'under control'.

A simulation approach is used to calculate confidence intervals for 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.

Perez-Reche FJ, Taylor N, McGuigan C, Conaglen P, Forbes K, Strachan N, Honhold N (2021) Estimated Dissemination Ratio — A practical alternative to the reproduction number for infectious diseases. Frontiers in Public Health 9. DOI: 10.3389/fpubh.2021.675065.

Examples

```
## EXAMPLE 1 Foot and mouth disease, Cumbria 2001:

## Counts of incident FMD positive farms in Cumbria by date:
edate <- seq(from = as.Date("2001-02-28", format = "%Y-%m-%d"),
   to = as.Date("2001-06-15", format = "%Y-%m-%d"), by = 1)
ncas <- c(1,2,0,0,1,1,0,0,4,2,3,3,5,2,8,2,5,0,5,7,15,13,6,7,11,8,7,11,
   6,5,10,7,8,8,7,5,6,3,3,3,3,4,1,4,6,2,1,4,3,3,1,1,1,2,2,2,2,0,4,1,1,
   0,0,2,1,2,1,0,1,2,2,4,0,1,0,1,0,0,0,1,0,3,1,1,3,0,0,1,1,2,0,0,1,1,1,
   3,3,1,1,1,0,0,0,1,1,1,1,1)
dat.df01 <- data.frame(edate = edate, ncas = ncas)


## Seven day EDR:
edr <- epi.edr(dat.df01$ncas, n = 7, conf.level = 0.95, nsim = 99,
   na.zero = FALSE)

dat.df01$edr.500 <- edr$est
dat.df01$edr.025 <- edr$lower
dat.df01$edr.975 <- edr$upper

## Smooth the EDRs:
dat.df01$sedr.500 <- lowess(dat.df01$edate, dat.df01$edr.500, f = 0.10)$y
dat.df01$sedr.025 <- lowess(dat.df01$edate, dat.df01$edr.025, f = 0.10)$y
dat.df01$sedr.975 <- lowess(dat.df01$edate, dat.df01$edr.975, f = 0.10)$y


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

## Frequency histogram of the number of incident FMD positive farms as a
## function of date:
```

```
ggplot() +
   theme_bw() +
   geom_histogram(data = dat.df01, aes(x = edate, weight = ncas),
      binwidth = 1, fill = "#008080", alpha = 0.45) +
   scale_x_date(breaks = date_breaks("7 days"),
      name = "Date of onset of signs") +
   scale_y_continuous(limits = c(0,20), name = "Number of events") +
   theme(axis.text.x = element_text(angle = 90, hjust = 1))


## EDR line plot (and its 95
## date. Set primary axis breaks and labels:
x <- 2^(-5:5)
y <- seq(from = 0, to = 20, length = length(x))
pybreaks <- y; pylabels <- x

ggplot() +
   theme_bw() +
   geom_line(data = dat.df01, aes(x = edate,
      y = 10 + (2 * log2(edr.500))), col = "black", linewidth = 1) +
   geom_line(data = dat.df01, aes(x = edate,
      y = 10 + (2 * log2(edr.025))), col = "black",
      linetype = "dashed", linewidth = 0.5) +
   geom_line(data = dat.df01, aes(x = edate,
      y = 10 + (2 * log2(edr.975))), col = "black",
      linetype = "dashed", linewidth = 0.5) +
   scale_x_date(breaks = date_breaks("7 days"),
      name = "Date of onset of signs") +
   scale_y_continuous(breaks = pybreaks, labels = pylabels,
      name = "Estimated dissemination ratio (EDR)") +
   coord_cartesian(xlim = range(dat.df01$edate), ylim = c(0,20)) +
   geom_hline(yintercept = 10, col = "red", linetype = "dashed") +
   theme(axis.text.x = element_text(angle = 90, hjust = 1))


## EDR line plot (and its 95
## date superimposed on the epidemic curve:

## Set the EDR values to appear on secondary vertical axis:
x <- 2^(-5:5)

## Set the number of FMD cases to appear on primary vertical axis:
y <- seq(from = 0, to = 20, length = length(x))

## Equation to use x (EDR estimate) to predict y (number of FMD cases):
dat.lm01 <- lm(y ~ log2(x))
summary(dat.lm01)

## Breaks and values for primary y axis:
pybreaks <- seq(from = 0, to = 20, by = 5)
pylabels <- pybreaks

## Breaks and values for secondary y axis:
```

```
sybreaks <- coefficients(dat.lm01)[1] + (coefficients(dat.lm01)[2] * log2(x))
sylabels <- x

ggplot() +
   theme_bw() +
   geom_histogram(data = dat.df01, aes(x = edate, weight = ncas),
      binwidth = 1, fill = "#008080", alpha = 0.45) +
   geom_line(data = dat.df01, aes(x = edate,
      y = 10 + (2 * log2(edr.500))), col = "black", linewidth = 1) +
   geom_line(data = dat.df01, aes(x = edate,
      y = 10 + (2 * log2(edr.025))), col = "black", linewidth = 0.5,
      linetype = "dashed") +
   geom_line(data = dat.df01, aes(x = edate,
      y = 10 + (2 * log2(edr.975))), col = "black", linewidth = 0.5,
      linetype = "dashed") +
   scale_x_date(breaks = date_breaks("1 month"),
      labels = date_format("%b %y"), name = "Date of onset of signs") +
   scale_y_continuous(breaks = pybreaks, labels = pylabels, limits = c(0,20),
      name = "Number of FMD cases",
      sec.axis = sec_axis(breaks = sybreaks, labels = sylabels,
      transform = ~ ., name = "Estimated dissemination ratio (EDR)")) +
   coord_cartesian(xlim = range(dat.df01$edate), ylim = c(0,20)) +
   geom_hline(yintercept = 10, col = "red", linetype = "dashed")

## End(Not run)
```

`epi.empbayes` *Empirical Bayes estimates of observed event counts*

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

```
## EXAMPLE 1:
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.df01 <- 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 = dat.df01, aes(x = rank, y = est, colour = Method)) +
  theme_bw() +
  geom_point() +
  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)) +
  scale_y_continuous(limits = c(0,30), name = "Lip cancer incidence rates
     (cases per 100,000 person years)")

## 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.evalue *Compute E-value for risk, rate, odds and hazard ratio estimates*

Description

Returns a list of the point estimate, lower confidence limit, and upper confidence limit for risk, rate, odds or hazard ratio (as provided by the user) and E-values for the measure of association point estimate and the confidence interval limit closer to the null.

Usage

```
epi.evalue(x, measure = "risk.ratio", rare = TRUE, conf.level = 0.95)
```

Arguments

x	an object of class glm, coxph or data.frame. If an object of class data.frame is provided the first column should be of class character listing the variable. Subsequent columns (2 to 4) should list (in order) the point estimate, the lower bound and the upper bound of the confidence interval of the measure of association.
measure	a character string indicating the measure used. Options are risk.ratio, rate.ratio, odds.ratio, or hazard.ratio.
rare	logical. If TRUE and measure = "odds.ratio" or measure = "hazard.ratio" it is assumed that the odds (or hazard) ratio are a valid approximation for the risk ratio.
conf.level	magnitude of the confidence interval provided in x. Must be a single number between 0 and 1.

Details

The E-value is the minimum strength of association, on the risk ratio scale, that an unmeasured confounder would need to have with both the exposure and the outcome to fully explain away a specific exposure-outcome association, conditional on the measured covariates included in a model (VanderWeele and Ding 2017). Larger E-values indicate that the observed association is more robust to potential unmeasured confounding.

It is usual to calculate the E-value for only the lower bound of the 95% CI when the risk ratio, odds ratio or hazard ratio is greater than 1 and for only the upper bound when the estimate is less than 1. The purpose of estimating the E-value of the 95% CI is to determine the strength of confounding required to bring the confidence limits of the risk ratio, odds ratio or hazard ratio to unity. That is, to make the estimate of the odds ratio, risk ratio or hazard ratio no longer statistically significant.

Value

When measure == "risk.ratio" or measure == "rate.ratio" a list containing:

rr	a data frame listing the variable name, the point estimate of the risk ratio, the lower bound of the confidence interval of the risk ratio and the upper bound of the confidence interval of the risk ratio, as entered by the user through argument x.
eval	a data frame listing est the E-value for the point estimate of the risk ratio (e.g., the estimated RR or OR), low the E-value for the confidence limit closest to the null (often called the minimum or CI-bound E-value) and upp the E-value for the confidence limit farthest from the null (sometimes called the maximum or outer-bound E-value).

When measure == "odds.ratio" a list containing:

or	a data frame listing the variable name, the point estimate of the odds ratio, the lower bound of the confidence interval of the odds ratio and the upper bound of the confidence interval of the odds ratio, as entered by the user through argument x.

`rr` a data frame listing the variable name, the point estimate of the risk ratio, the lower bound of the confidence interval of the risk ratio and the upper bound of the confidence interval of the risk ratio, computed using the odds ratio estimates entered by the user through argument `x`.

`eval` a data frame listing `est` the E-value for the point estimate of the risk ratio (e.g., the estimated RR or OR), `low` the E-value for the confidence limit closest to the null (often called the minimum or CI-bound E-value) and `upp` the E-value for the confidence limit farthest from the null (sometimes called the maximum or outer-bound E-value).

When `measure == "hazard.ratio"` a list containing:

`hr` a data frame listing the variable name, the point estimate of the hazard ratio, the lower bound of the confidence interval of the hazard ratio and the upper bound of the confidence interval of the hazard ratio, as entered by the user through argument `x`.

`rr` a data frame listing the variable name, the point estimate of the risk ratio, the lower bound of the confidence interval of the risk ratio and the upper bound of the confidence interval of the risk ratio, computed using the hazard ratio estimates entered by the user through argument `x`.

`eval` a data frame listing `est` the E-value for the point estimate of the risk ratio (e.g., the estimated RR or OR), `low` the E-value for the confidence limit closest to the null (often called the minimum or CI-bound E-value) and `upp` the E-value for the confidence limit farthest from the null (sometimes called the maximum or outer-bound E-value).

References

Ding P, VanderWeele T, (2016) Sensitivity analysis without assumptions. Epidemiology 27: 368 - 377.

VanderWeele TJ, Ding P (2017). Sensitivity analysis in observational research: Introducing the E-value. Annals of Internal Medicine 167: 268 - 274.

Examples

```
## EXAMPLE 1:
## The birthwt data frame from the MASS package were collected at Baystate
## Medical Center, Springfield, Massachusetts USA in 1986. A logistic
## regression model is run to quantify the effect of smoking during pregancy
## and delivery of a low birth weight baby, controlling for the effect of race.

library(MASS)
dat.df <- birthwt; head(dat.df)
dat.glm <- glm(low ~ smoke + race, family = binomial, data = dat.df)
table(dat.df$low)

## The study outcome (low birthweight) is relatively common so we set rare =
## FALSE
```

```
epi.evalue(x = dat.glm, measure = "odds.ratio", rare = FALSE,
   conf.level = 0.95)

## $or
##     var      est    lower    upper
## 1 smoke 3.054692 1.507644 6.432485
## 2  race 1.748883 1.196771 2.611134

## $rr
##     var      est    lower    upper
## 1 smoke 1.747768 1.227861 2.536234
## 2  race 1.322453 1.093970 1.615900

## $eval
##     var      est    lower upper
## 1 smoke 2.890975 1.756806    NA
## 2  race 1.975469 1.414596    NA

## After controlling for the effect of race, the odds of delivering a low
## birth weight baby for smokers was 3.05 (95% CI 1.51 to 6.43) times that of
## non-smokers.

## After controlling for the effect of race, the risk of delivering a low
## birth weight baby for smokers was 1.75 (95% CI 1.23 to 2.53) times that of
## non-smokers.

## An unmeasured confounder in this study would need to be associated with both
## smoking and delivery of a low birth weight baby by a risk ratio of at
## least 2.89 each, above and beyond the measured covariates, to completely
## explain the observed risk ratio of 1.75.

## The E-value for the lower confidence limit is 1.76. To reduce the
## association enough that the lower bound of the risk ratio confidence limit
## (1.23) would include the null, an unmeasured confounder would still need
## to have associations of about 1.76 with both the exposure and the outcome.
```

`epi.fpos` *Calculate the expected number of false positive and false negative test results*

Description

Compute the number of true positives, false positives, true negatives and false negatives given the number of individuals tested, the design prevalence and diagnostic test sensitivity and specificity.

Usage

```
epi.fpos(n, pstar, se.u, sp.u, conf.level = 0.95)
```

Arguments

n	scalar, integer, the number of surveillance units tested.
pstar	scalar, the expected design prevalence.
se.u	scalar, the surveillance unit sensitivity.
sp.u	scalar, the surveillance unit specificity.
conf.level	magnitude of the returned confidence interval. Must be a single number between 0 and 1.

Value

A list containing the following:

test.pos	the expected median number of test positives and the uncertainty in the number of test positives, as specified by conf.level.
true.pos	the expected median number of true positives and the uncertainty in the number of true positives, as specified by conf.level.
false.pos	the expected median number of false positives units and the uncertainty in the number of false positives, as specified by conf.level.
test.neg	the expected median number of test negatives and the uncertainty in the number of test negative, as specified by conf.level.
true.neg	the expected median number of true negatives and the uncertainty in the number of true negative, as specified by conf.level.
false.neg	the expected median number of false negatives and the uncertainty in the number of false negative, as specified by conf.level.

Examples

```
## EXAMPLE 1:
## A bulk milk tank test has been developed to detect bovine tuberculosis
## (bTB) in dairy herds. The diagnostic sensitivity and specificity of the
## test is 0.714 and 0.981, respectively.

## If there are 9,000 dairy herds in the population of interest and of that
## group 15 are thought to be bTB positive how many false positive test
## results can be expected if all herds are tested on a single occasion?

epi.fpos(n = 9000, pstar = 15 / 9000, se.u = 0.714, sp.u = 0.981,
   conf.level = 0.95)$false.pos

## If all 9,000 herds are tested on a single occasion we can expect 171
## (95% CI 146 to 197) false positive.

## How many false negatives are expected using this test regime?

epi.fpos(n = 9000, pstar = 15 / 9000, se.u = 0.714, sp.u = 0.981,
   conf.level = 0.95)$false.neg

## If all 9,000 herds are tested on a single occasion we can expect 4
## (95% CI 1 to 9) false negatives.
```

`epi.herdtest` *Estimate the characteristics of diagnostic tests applied at the herd (group) level*

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 list with one scalar and two data frames.

Scalar `sfraction` reports the sampling fraction (i.e., `n / N`). The binomial distribution is recommended if `sfraction` is less than 0.2.

Data frame `dbinom` lists `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 calculated using the binomial distribution.

Data frame `dhyper` lists `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 calculated using the hypergeometric.

Author(s)

Ron Thornton, MPI 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 want 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 0.99 and a herd
## specificity of 0.36 (using the binomial distribution). With a herd
## sensitivity of 0.95 we can be confident that we will declare a herd
## as disease positive if it truly is disease positive. 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 explanatory variable 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 (or 'reference') 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 explanatory variables 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 when stratum-specific incidence risk estimates are 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 calculated using the Ulm (1990) method.

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.

Lash TL, VanderWeele TJ, Haneuse S, Rothman KJ (2021). Modern Epidemiology. Lippincott - Raven Philadelphia, USA, pp. 75.

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.

Ulm K (1990) A simple method to calculate the confidence interval of a standardized mortality ratio. American Journal of Epidemiology 131: 373 - 375. DOI: 10.1093/oxfordjournals.aje.a115507

See Also

epi.directadj

Examples

```
## EXAMPLE 1 (without covariates):
## Adapted from Dohoo, Martin and Stryhn (2009). Data have been collected on
## the incidence of tuberculosis (TB) )positive herds in two areas ("A" and
## "B"). Provided are the counts of incident TB positive herds and counts
## of the herd population at risk. The herd level TB incidence risk for this
## population is 0.060 (6 TB positive herds per 100 herds at risk).

## In their text Dohoo et al. present this example as incidence rate data
## (the number of TB positive herds per herd-year at risk). For this example
## the frequency of tuberculosis is expressed as an incidence risk
## (i.e., the number of TB positive herds divided by the size of the herd
## population at risk).

obs.m01 <- matrix(data = c(58,130), nrow = 2, byrow = TRUE,
```

```
   dimnames = list(c("A","B"), ""))
pop.m01 <- matrix(data = c(1000,2000), nrow = 2, byrow = TRUE,
   dimnames = list(c("A","B"), ""))
std.m01 <- 0.060

epi.indirectadj(obs = obs.m01, pop = pop.m01, std = std.m01, units = 100,
   conf.level = 0.95)

## In area A the observed number of TB positive herds was 0.97 (95% CI
## 0.73 to 1.25) times the number expected. In area B the observed number
## of TB positive herds was 1.1 (95% CI 0.90 to 1.3) times the number expected.

## EXAMPLE 2 (with covariates):
## We now have, for each area, the data stratified by herd type (dairy, beef).
## The incidence risks of TB for beef herds, dairy herds and the
## total population are 0.025, 0.085, and 0.060 (2.5, 8.5 and 6.0 TB positive
## herds per 100 herds at risk), respectively:

obs.m02 <- matrix(data = c(58,130), nrow = 2, byrow = TRUE,
   dimnames = list(c("A","B"), ""))
pop.m02 <- matrix(data = c(550,450,500,1500), nrow = 2, byrow = TRUE,
   dimnames = list(c("A","B"), c("Beef","Dairy")))
std.m02 <- matrix(data = c(0.025,0.085,0.060), nrow = 1, byrow = TRUE,
   dimnames = list("", c("Beef","Dairy","Total")))

epi.indirectadj(obs = obs.m02, pop = pop.m02, std = std.m02, 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 0.8469583 1.441893
## > B 130 140 0.9285714 0.7758190 1.102603

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

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

epi.insthaz *Event instantaneous hazard based on Kaplan-Meier survival estimates*

Description

Compute event 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 the event of interest, equivalent to the proportion of the group at risk failing per unit time.

Value

A data frame with the following variables: strata the strata identifier, time the observed event times, n.risk the number of individuals at risk at the start of the event time, n.event the number of individuals that experienced the event of interest at the event time, n.censor the number of individuals censored at the event time, sest the observed Kaplan-Meier survival estimate at the event time, slow the lower bound of the confidence interval for the observed Kaplan-Meier survival estimate at the event time, supp the upper bound of the confidence interval for the observed Kaplan-Meier survival estimate at the event time, hest the observed instantaneous hazard at the event time, hlow the lower bound of the confidence interval for the observed instantaneous hazard at the event time, and hupp the upper bound of the confidence interval for the observed instantaneous hazard at the event time.

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

```
## EXAMPLE 1:
library(survival)
lung.df01 <- lung

lung.df01$status <- ifelse(lung.df01$status == 1, 0, lung.df01$status)
lung.df01$status <- ifelse(lung.df01$status == 2, 1, lung.df01$status)
lung.df01$sex <- factor(lung.df01$sex, levels = c(1,2),
   labels = c("Male","Female"))

lung.km01 <- survfit(Surv(time = time, event = status) ~ 1, data = lung.df01)
lung.haz01 <- epi.insthaz(survfit.obj = lung.km01, conf.level = 0.95)

lung.shaz01 <- data.frame(
  time = lowess(lung.haz01$time, lung.haz01$hlow, f = 0.20)$x,
  shest =  lowess(lung.haz01$time, lung.haz01$hest, f = 0.20)$y,
  shlow =  lowess(lung.haz01$time, lung.haz01$hlow, f = 0.20)$y,
  shupp =  lowess(lung.haz01$time, lung.haz01$hupp, f = 0.20)$y)

## What was the maximum follow-up time? Use this to guide limits for the
## horizontal axis:
summary(lung.haz01$time)

## Maximum follow up time 883 days, so set horizontal axis limit to a
## bit less, say 800 days. This will avoid instability in the smoothed results
## at the extremes of the data.

plot(x = lung.haz01$time, y = lung.haz01$hest, xlab = "Time (days)",
   ylab = "Daily probability of event", type = "s",
   col = "grey", xlim = c(0,800), ylim = c(0, 0.05))
lines(x = lung.shaz01$time, y = lung.shaz01$shest,
      lty = 1, lwd = 2, col = "black")
lines(x = lung.shaz01$time, y = lung.shaz01$shlow,
      lty = 2, lwd = 1, col = "black")
lines(x = lung.shaz01$time, y = lung.shaz01$shupp,
      lty = 2, lwd = 1, col = "black")

## Not run:
library(ggplot2)

ggplot() +
  theme_bw() +
  geom_step(data = lung.haz01, aes(x = time, y = hest), colour = "grey") +
  geom_line(data = lung.shaz01, aes(x = time, y = shest), colour = "black",
     linewidth = 0.75, linetype = "solid") +
  geom_line(data = lung.shaz01, aes(x = time, y = shlow), colour = "black",
     linewidth = 0.50, linetype = "dashed") +
  geom_line(data = lung.shaz01, aes(x = time, y = shupp), colour = "black",
     linewidth = 0.50, linetype = "dashed") +
  scale_x_continuous(limits = c(0,800), name = "Time (days)") +
  scale_y_continuous(limits = c(0,0.10), name = "Daily probability of event")
```

```
## End(Not run)


## EXAMPLE 2:
## Stratify the analyses by sex:
lung.km02 <- survfit(Surv(time = time, event = status) ~ sex, data = lung.df01)
lung.haz02 <- epi.insthaz(survfit.obj = lung.km02, conf.level = 0.95)

## Split the data by sex:
lung.split02 <- split(x = lung.haz02, f = lung.haz02$strata)

## Loess smooth teh data for each group using lapply:
lung.loess02 <- lapply(X = lung.split02, FUN = function(dat, span = 0.4) {
   hest <- loess(hest ~ time, data = dat, span = span)$fit
   hlow <- loess(hlow ~ time, data = dat, span = span)$fit
   hupp <- loess(hupp ~ time, data = dat, span = span)$fit
  data.frame(strata = dat$strata, time = dat$time, hest = hest,
   hlow = hlow, hupp = hupp)
})

## Combine the loess smoothed results into a single data frame:
lung.shaz02 <- do.call(rbind, lung.loess02)
row.names(lung.shaz02) <- NULL

## Not run:
library(ggplot2)

## Use the same horizontal axis limits calculated above:
ggplot() +
  theme_bw() +
  geom_step(data = lung.haz02, aes(x = time, y = hest), colour = "grey") +
  facet_grid(strata ~ .) +
  geom_ribbon(data = lung.shaz02, aes(x = time, ymin = hlow, ymax = hupp),
     alpha = 0.25) +
  scale_x_continuous(limits = c(0,800), name = "Time (days)") +
  scale_y_continuous(limits = c(0,0.10), name = "Daily probability of event")

## End(Not run)
```

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

Description

For two binary explanatory variables included in a logistic regression as an interaction term, computes the relative excess risk due to interaction, the proportion of outcomes among those with both exposures attributable to interaction, and the synergy index. Confidence interval calculations are based on the delta method described by Hosmer and Lemeshow (1992).

Usage

```
epi.interaction(model, coef, param = c("product", "dummy"), conf.level = 0.95)
```

Arguments

model	an object of class glm, geeglm, glmerMod, clogit or coxph.
coef	a vector of length three listing the positions of the coefficients of the interaction terms in the model. What row numbers of the regression table summary list the coefficients for the interaction terms included in the model?
param	a character string specifying the type of coding used for the variables included in the interaction term. Options are product where two (dichotomous) explanatory variables and one product term are used to represent the interaction and dummy where the two explanatory variables are combined into a single explanatory variable comprised of four levels. See the examples, below, for details.
conf.level	magnitude of the returned confidence interval. Must be a single number between 0 and 1.

Details

Interaction on an additive scale means that the combined effect of two exposures is greater (or less) than the sum of the individual effects of two exposures. Interaction on a multiplicative scale means that the combined effect of the two exposures is greater (or less) than the product of the individual effects of the two exposures.

This function calculates three indices to assess the presence of additive interaction, as defined by Rothman (1998): (1) the relative excess risk due to interaction (RERI, sometimes called the interaction contrast ratio), (2) the proportion of disease among those with both exposures that is attributable to their interaction (AP[AB]), and (3) the synergy index (S).

If at least one of the two exposures are preventive (i.e., ORs of less than one) then the estimate of SI will be invalid (RERI and AP remain unaffected). In this situation the function issues an appropriate warning. To estimate SI the exposures need to be recoded so the stratum with the lowest outcome risk becomes the new reference category when the two exposures are considered together.

A RERI of zero means no additive interaction. A RERI of greater than one means positive interaction or more than additivity. A RERI of less than one means negative interaction or less than additivity. RERI ranges from zero to infinity.

An AP[AB] of zero means no interaction or exactly additivity. An AP[AB] greater than zero means positive interaction or more than additivity. An AP[AB] of less than zero means negative interaction or less than additivity. AP[AB] ranges from -1 to +1.

The synergy index is the ratio of the combined effects and the individual effects. An S of one means no interaction or exactly additivity. An S of greater than one means positive interaction or more than additivity. An S of less than one means negative interaction or less than additivity. S ranges from zero to infinity.

In the absence of interaction AP[AB] = 0 and RERI and S = 1.

Skrondal (2003) advocates for use of the synergy index as a summary measure of additive interaction, showing that when regression models adjust for the effect of confounding variables (as in the majority of cases) RERI and AP may be biased, while S remains unbiased.

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 details.

A measure of multiplicative interaction is `RR11 / (RR10 * RR01)`. If `RR11 / (RR10 * RR01)` equals one multiplicative interaction is said to be absent. If `RR11 / (RR10 * RR01)` is greater than one multiplicative interaction is said to be positive. If `RR11 / (RR10 * RR01)` is less than one multiplicative interaction is said to be negative.

Value

A list containing:

`reri`	the point estimate and lower and upper bounds of the confidence interval for the relative excess risk due to interaction, RERI.
`apab`	the point estimate and lower and upper bounds of the confidence interval for the proportion of disease among those with both exposures that is attributable to their interaction, APAB.
`s`	the point estimate and lower and upper bounds of the confidence interval for the synergy index.
`multiplicative`	the point estimate and lower and upper bounds of the confidence interval for the odds ratio for multiplicative interaction.

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.

Knol MJ, VanderWeele TJ (2012). Recommendations for presenting analyses of effect modification and interaction. International Journal of Epidemiology 41: 514 - 520.

Lash TL, VanderWeele TJ, Haneuse S, Rothman KJ (2021). Modern Epidemiology. Lippincott - Raven Philadelphia, USA, pp. 621 - 623.

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.

VanderWeele TJ, Knol MJ (2014). A tutorial on interaction. Epidemiologic Methods 3: 33 - 72.

Examples

```
## EXAMPLE 1:
## Data from Rothman and Keller (1972) evaluating the effect of joint exposure
## to smoking and alcohol use on the 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.df01 <- data.frame(alc, smk, can)

## Table 2 of Hosmer and Lemeshow (1992):
dat.glm01 <- glm(can ~ alc + smk + alc:smk, family = binomial, data = dat.df01)
summary(dat.glm01)

## What is the measure of effect modification on the additive scale?
epi.interaction(model = dat.glm01, param = "product", coef = c(2,3,4),
   conf.level = 0.95)$reri

## Measure of interaction on the additive scale: RERI 3.73
## (95% CI -1.84 to 9.32), page 453 of Hosmer and Lemeshow (1992).

## What is the measure of effect modification on the multiplicative scale?
## See VanderWeele and Knol (2014) page 36 and Knol and Vanderweele (2012)
## for details.
epi.interaction(model = dat.glm01, param = "product", coef = c(2,3,4),
   conf.level = 0.95)$multiplicative
## Measure of interaction on the multiplicative scale: 0.091 (95% CI 0.14 to
## 5.3).


## EXAMPLE 2:
## 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 comprised of
## (in this case) four levels. Dummy variables are added to the data set using
## the following code:

## 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.df01$d <- rep(NA, times = nrow(dat.df01))
dat.df01$d[dat.df01$alc == 0 & dat.df01$smk == 0] <- 0
dat.df01$d[dat.df01$alc == 1 & dat.df01$smk == 0] <- 1
dat.df01$d[dat.df01$alc == 0 & dat.df01$smk == 1] <- 2
dat.df01$d[dat.df01$alc == 1 & dat.df01$smk == 1] <- 3
dat.df01$d <- factor(dat.df01$d)

## Table 3 of Hosmer and Lemeshow (1992):
dat.glm02 <- glm(can ~ d, family = binomial, data = dat.df01)
summary(dat.glm02)
```

```
## What is the measure of effect modification on the additive scale?
epi.interaction(model = dat.glm02, param = "dummy", coef = c(2,3,4),
   conf.level = 0.95)

## Measure of interaction on the additive scale: RERI 3.74
## (95% CI -1.84 to 9.32), page 455 of Hosmer and Lemeshow (1992).


## EXAMPLE 3:
## Here we demonstrate the use of epi.interaction when you're working with
## multilevel data. Imagine each of the study subjects listed in data frame
## dat.df01 are aggregated into clusters (e.g., community health centres).
## Assuming there are five clusters, assign each subject to a cluster:

## Not run:
set.seed(1234)
dat.df01$inst <- round(runif(n = nrow(dat.df01), min = 1, max = 5), digits = 0)
table(dat.df01$inst)

## Fit a generalised linear mixed-effects model using function glmer in the
## lme4 package, with variable inst as a random intercept term:

dat.glmer01 <- glmer(can ~ alc + smk + alc:smk + (1 | inst), family = binomial,
   data = dat.df01)
summary(dat.glmer01)

## What is the measure of effect modification on the additive scale?
epi.interaction(model = dat.glmer01, param = "product", coef = c(2,3,4),
   conf.level = 0.95)

## Measure of interaction on the additive scale: RERI 3.74
## (95% CI -1.84 to 9.32), identical to that produced above largely because
## there's no strong institution-level effect due to the contrived way we've
## created the multilevel data.

## End(Not run)
```

`epi.iref` *Calculate diagnostic sensitivity and specificity using an imperfect reference test*

Description

Calculate diagnostic sensitivity and specificity using an imperfect reference test.

Usage

```
epi.iref(x, se.rs, sp.rs, method = "staquet", ci.method = "wilson",
   conf.level = 0.95, warn = TRUE)
```

Arguments

x	a vector of length four, an object of class table or an object of class grouped_df from package dplyr containing the individual cell frequencies (see below).
se.rs	scalar, the known diagnostic sensitivity of the reference test. Must be a single number between 0 and 1.
sp.rs	scalar, the known diagnostic specificity of the reference test. Must be a single number between 0 and 1.
method	character string indicating the method to use. Options are brenner, gart_buck, or staquet.
ci.method	character string indicating the confidence interval calculation method to use. For method == "gart_buck" and method = "staquet" options are wilson anddelta. For method == "brenner" options are wilson and wilson.eff.
conf.level	magnitude of the confidence interval of the sensitivity and specificity estimates. Must be a single number between 0 and 1.
warn	logical. If TRUE warnings are issued in the event of input data irregularities.

Details

The required 2 by 2 table format for argument x for epi.iref is shown below. Columns list counts for the reference test: counts of test positive study units in column 1 and test negative study units in column 2. Rows list counts for the index test (i.e., the test under investigation): counts of test positive study units in row 1 and counts of test negative study units in row 2. The labels a, b, c and d in the table below correspond to the order of study unit counts when argument dat is a vector.

	Reference +	Reference -	Total
Test +	a	b	a + b
Test -	c	d	c + d
Total	a + c	b + d	a + b + c + d

Value

A list containing the following:

uncorrected	diagnostic sensitivity and specificity for the index test (and their confidence intervals), computed using the values provided in table x.
uncorrected	diagnostic sensitivity and specificity for the index test (and their confidence intervals) computed using the reference test as a quasi gold standard.
prevalence	apparent prevalence and true prevalence (and their confidence intervals) computed using the reference test as the quasi gold standard.

Note

The diagnostic accuracy measures (sensitivity and specificity) of a new test can be estimated by comparing test results to a gold standard.

Brenner (1996), Gart and Buck (1996), and Staquet et al. (1981) have published methods to estimate the sensitivity and specificity of a binary response index test when the sensitivity and specificity of the imperfect reference standard are known and the index test and reference standard are conditionally independent.

Based on a methodological review by Chikere et al. (2021), under the assumption of conditional independence, the Staquet et al. correction method outperforms the Brenner correction method irrespective of the prevalence of disease and whether the performance of the reference standard is better or worse than the index test. When the prevalence of the disease is high (> 0.9) or low (< 0.1), the Staquet et al. correction method can produce illogical results (i.e., results outside [0,1]). When the two tests are dependent both methods fail to estimate the sensitivity and specificity of the index test particularly when the covariance terms between the index test and the reference standard is not close to zero.

This function will be of most use in the situation when investigators have compared the results of an index test to an imperfect reference standard and calculated sensitivity and specificity, labelling them as 'relative' sensitivity and specificity estimates. On the condition that: (1) the diagnostic sensitivity and specificity of the imperfect reference test is known (i.e., the test has been validated against a gold standard); and (2) the prevalence of disease is within the range of approximately 0.1 to 0.9 (see above) this function is useful to (quickly) show how how far relative diagnostic sensitivity and specificity estimates are from 'actual' sensitivity and specificity estimates. Bayesian latent class modelling is the recommended approach to determine the diagnostic sensitivity and specificity of a test in the absence of a gold standard.

Author(s)

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References

Brenner H (1996). Correcting for exposure misclassification using an alloyed gold standard. Epidemiology 7: 406 - 410.

Gart J, Buck A (1966). Comparison of a screening test and a reference test in epidemiologic studies. II. A probabilistic model for the comparison of diagnostic tests. American Journal of Epidemiology 83: 593 - 602. DOI: 10.1093/oxfordjournals.aje.a120610.

Habibzadeh F (2023). On determining the sensitivity and specificity of a new diagnostic test through comparing its results against a non-gold-standard test. Biochemia Medica: Casopis Hrvatskoga Drustva Medicinskih Biokemicara 33, 010101. DOI: 10.11613/BM.2023.010101.

Staquet M, Rozencweig M, Lee Y, Muggia F (1981). Methodology for the assessment of new dichotomous diagnostic tests. Journal of Chronic Diseases 34, 599 - 610. DOI: 10.1016/0021-9681(81)90059-x.

Chikere C, Wilson K, Allen A, Vale L (2021). Comparative diagnostic accuracy studies with an imperfect reference standard — a comparison of correction methods. BMC Medical Research Methodology 21: 67. DOI: 10.1186/s12874-021-01255-4.

Examples

```
## EXAMPLE 1 (from Habibzadeh 2023):
## The results of a new (index) diagnostic test were compared with an existing
## reference. Of 150 individuals that were positive to the reference test, 107
## were positive to the index test. Of 450 individuals that were negative
## to the reference test, 104 were positive to the index test. The known
## sensitivity of the reference test is 0.850. The known specificity of the
## reference test is 0.900.

## What is the diagnostic sensitivity and specificity of the index test?

x <- c(107,104,43,346)
epi.iref(x = x, se.rs = 0.850, sp.rs = 0.900, method = "staquet",
   ci.method = "wilson", conf.level = 0.95, warn = TRUE)

## Without correction (i.e., assuming the reference test has perfect
## diagnostic sensitivity and specificity) the sensitivity and specificity of
## the index test is 0.71 (95% CI 0.63 to 0.78) and 0.77 (95% CI 0.73 to
## 0.81), respectively.

## With correction (i.e., accounting for imperfect performance of the reference
## test) the sensitivity and specificity of the index test is 0.95 (95% CI
## 0.91 to 0.98) and 0.80 (95% CI 0.76 to 0.83), respectively.
```

---

epi.iv *Fixed-effects 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

```
## EXAMPLE 1:
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 matrix comprised of n rows and n columns listing the individual cell frequencies (as integers).
method	a character string indicating the method to use. Options are fleiss, fleiss.everitt, watson, altman or cohen.
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 (Byrt 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. Bias and prevalence adjusted kappa are only returned if the number of rows and columns of argument `dat` are equal to 2.

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 (Sim and Wright, 2005).

PABAK (the prevalence and bias corrected kappa statistic) is calculated using the overall proportion of observed agreement. Confidence intervals for the overall proportion of observed agreement calculated using the exact method (Collett 1999). For this reason you won't see a change in the confidence intervals for PABAK when different settings are used for argument `method`.

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

Method `fleiss.everitt` provides confidence intervals that are appropriate when kappa is far from zero, based on Fleiss et al. (1969), formula 8.

Value

Where the number of rows and columns of argument `dat` is greater than 2 a list containing the following:

`prop.agree`	a data frame with `obs` the observed proportion of agreement and `exp` the expected proportion of agreement.
`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.

Where the number of rows and columns of argument `dat` is equal to 2 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.
max.kappa	a data frame listing the maximum attainable kappa, the standard error of the maximum attainable kappa and the lower and upper bounds of the confidence interval for the the maximum attainable kappa.
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 (2012, p 167 equation 9-2) 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 (2012, p 167 equation 9-2) for details.

The maximum kappa represents the greatest possible kappa value within the unchanged marginal totals (Graham 1992; Sim and Wright 2005). This method is used to understand the upper bound of agreement between examiners. Because the marginal totals are fixed, when the difference between kappa and maximum kappa is high, individual examiner tendencies, assessment methods, or differences in assessment methods should be considered as relevant sources of disagreement. When there is a marked difference between kappa and maximum kappa, kappa values should be interpreted with caution.

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

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Chen G, Faris P, Hemmelgarn B, Walker R, Quan H, (2009). Measuring agreement of administrative data with chart data using prevalence unadjusted and adjusted kappa. BMC Medical Research Methodology 9: 5. DOI: 10.1186/1471-2288-9-5.

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Kowalska M, Holz N, Pot S, Rampazzo A, Hartnack S (2026) Challenges and misinterpretations of Cohen's kappa in agreement studies in ophthalmology. Veterinary Ophthalmology 29: e70208. DOI: 10.1111/vop.70208.

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Sim J, Wright CC (2005) The kappa statistic in reliability studies: Use, interpretation, and sample size requirements. Physical Therapy 85: 257 - 268. DOI: 10. 1093/ ptj/ 85.3. 257.

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.m01 <- matrix(c(19,10,6,256), nrow = 2, byrow = TRUE)
colnames(dat.m01) <- c("L1-pos","L1-neg")
rownames(dat.m01) <- c("L2-pos","L2-neg")

dat.kap01 <- epi.kappa(dat.m01, method = "fleiss", alternative = "greater",
   conf.level = 0.95)
dat.kap01

## 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 agreement 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.

## The prevalence and bias corrected kappa statistic (PABAK) is 0.89
## (95% CI 0.82 to 0.94).

## Compare Fleisss confidence intervals for kappa with Fleiss-Everitt
## confidence intervals:
dat.m02 <- dat.m01
dat.kap02 <- epi.kappa(dat.m02, method = "fleiss.everitt",
   alternative = "greater", conf.level = 0.95)

dat.kap01$kappa
dat.kap02$kappa


## 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.m03 <- matrix(c(596,61,29,987), nrow = 2, byrow = TRUE)
colnames(dat.m03) <- c("US-pos","US-neg")
rownames(dat.m03) <- c("ELISA-pos","ELISA-neg")
```

```
dat.kap03 <- epi.kappa(dat.m03, method = "watson", alternative = "greater",
   conf.level = 0.95)
dat.kap03$kappa

## 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.

dat.kap03$pabak

## The prevalence and bias corrected kappa statistic (PABAK) is 0.89
## (95% CI 0.87 to 0.91).


## EXAMPLE 3 (from Kowalska et al. 2026):
## In pre-breeding assessments the European College of Veterinary
## Ophthamology Hereditary Eye Diseases) gonioscopy grading scheme is
## typically undertaken by a single ophthalmologist. The study by Holz et al.
## (2026) aimed to evaluate inter-examiner agreement using this grading
## scheme. Two ophthalmologists with similar clinical expertise independently
## assessed 60 dogs using the ECVO- HED 2022 gonioscopy grading scheme and its
## guidelines for evaluating the iridocorneal angle. The following results
## were obtained for left eyes (Table 4, Kowalska et al. 2026):

dat.m04 <- matrix(c(52,6,1,1), nrow = 2, byrow = TRUE)
colnames(dat.m04) <- c("Pass","Fail")
rownames(dat.m04) <- c("Pass","Fail")

dat.kap04 <- epi.kappa(dat = dat.m04, method = "fleiss",
   alternative = c("two.sided"), conf.level = 0.95)

dat.kap04$kappa
dat.kap04$kappa.max

## Cohen's kappa: 0.18 (95% CI -0.02 to 0.38)
## Maximum kappa: 0.41 (95% CI -0.08 to 0.90)
```

`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)

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References

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

Examples

```
## EXAMPLE 1:
## 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.df01 <- data.frame(ckey, pkey, lact, dim, llen, vol, fat, pro)

## Lactation to date and 305-day milk, fat, and protein yield:
epi.ltd(dat.df01, std = "305")

## Lactation to date and 270-day milk, fat, and protein yield:
```

```
epi.ltd(dat.df01, std = "270")
```

---

epi.mbf *Minimum Bayes factor using the Goodman or Sellke et al. method.*

Description

A function to calculate the minimum Bayes factor using the Goodman or Sellke et al. method.

Usage

```
epi.mbf(H0, class = c("prior", "posterior"), p, method = c("goodman", "sellke"),
   two.sided = TRUE)
```

Arguments

H0	scalar, prior or posterior estimate of the null hypothesis being true.
class	character, prior or posterior.
p	scalar, the p-value calculated for the comparison of interest.
method	character, which minimum Bayes factor calculation method to use. Options goodman or sellke. See details, below.
two.sided	logical, if TRUE the analysis assumes a two-sided test has been used.

Details

A Bayes factor is a number that tells you how much a piece of evidence should shift your belief between two competing explanations such as: 'this treatment works' versus 'ths treatment doesn't work'.

The 'minimum' Bayes factor is the smallest possible shift in belief that a given piece of evidence (like a p-value from a study) could justify, even under the most generous assumptions favouring the surprising result. It is used to show that even seemingly strong evidence (such as a low p-value) often provides weaker support for a hypothesis than people intuitively assume, because it calculates the best-case scenario for that evidence and often still finds it underwhelming.

The Goodman (1999) method compares the null hypothesis to a single, specific alternative: The value of the parameter that best fits the data (the maximum likelihood estimate).

The Sellke, Bayarri and Berger (2001) method considers an entire class of reasonable prior distributions on the alternative hypothesis (essentially, any distribution that doesn't put special weight right at the null) and finds the minimum Bayes factor across that whole class.

The Sellke, Bayarri and Berger method is consistently more conservative (larger minimum Bayes factor estimates, i.e., weaker evidence against the null) than the Goodman method. This makes sense: the Goodman method is comparing against the single best-fitting alternative, which is the most favourable comparison possible. The Sellke-Bayarri-Berger method asks for the worst case across many reasonable alternatives, which can't be as extreme as cherry-picking the one alternative that happens to match the data perfectly.

Value

A list containing the following:

method	the minimum Bayes factor method (goodman or sellke) as entered by the user.
H0.prior	the prior estimate that the null hypothesis is true. If class is set to prior this is the value of H0 entered by the user. If class is set to posterior this is the minimum Bayes factor estimate of H0.
H1.prior	the prior estimate that the alternative hypothesis is true. If class is set to prior this is 1 minus the value of H0 entered by the user. If class is posterior this is 1 - the minimum Bayes factor estimate of H0.
H0.post	the posterior estimate that the null hypothesis is true. If class is set to prior this is minimum Bayes factor estimate of H0. If class is set to posterior this is the value of H0 entered by the user.
H1.post	the posterior estimate that the alternative hypothesis is true. If class is set to prior this is 1 minus the minimum Bayes factor estimate of H0. If class is set to posterior this is 1 minus the value of H0 entered by the user.
interp	a one sentence statement of the results.

References

Goodman S (1999) Toward evidence-based medical statistics. 1: The P value fallacy. Annals of Internal Medicine 130: 995 - 1004. DOI: 10.7326/0003-4819-130-12-199906150-00008.

Sellke T, Bayarri M, Berger J (2001) Calibration of p values for testing precise null hypotheses. American Statistician 55: 62 - 71.

Examples

```
## EXAMPLE 1:
## A pharmaceutical company tests a new blood pressure medication against a
## placebo in a clinical trial with 200 patients. At the start of the trial
## the researchers are moderately optimistic. Previous research on similar
## compounds suggests the drug probably works, but there's real uncertainty.
## They set their prior probability that H1 (the drug is effective) is true
## at 0.60.

## The trial finds a statistically significant reduction in blood pressure
## in the treatment group, with a p-value of 0.04.

epi.mbf(H0 = 0.40, class = "prior", p = 0.04, method = "goodman",
   two.sided = TRUE)

## The calculated minimum Bayes factor is 0.121. With a prior estimate of the
## probability that H1 is true of 0.6 the data provide at most a posterior
## probability of 0.925 in favour of H1.

## Repeat these calculations using the Sellke, Bayarri and Berger method:

epi.mbf(H0 = 0.40, class = "prior", p = 0.04, method = "sellke",
   two.sided = TRUE)
```

```
## The calculated minimum Bayes factor is 0.350. With a prior estimate of the
## probability that H1 is true of 0.6 the data provide at most a posterior
## probability of 0.811 in favour of H1.
```

`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

```
## EXAMPLE 1:
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 an outcome given diagnostic test sensitivity and specificity*

Description

Compute the post-test probability of an outcome given diagnostic test sensitivity and specificity.

Usage

```
epi.nomogram(pretest.ppos, se, sp, lratio.pos = NA, lratio.neg = NA,
   tconf.int = 0.95, method = "exact", verbose = FALSE, cred.int = 0.95,
   nsim = 999)
```

Arguments

pretest.ppos	the pre-test probability of being outcome positive (0 - 1).
se	diagnostic test sensitivity (0 - 1). Either a vector of length one listing the point estimate of the diagnostic test sensitivity or a vector of length three listing (in order) the point estimate, the lower bound of the confidence interval and the upper bound of the confidence interval of the diagnostic test sensitivity.
sp	diagnostic test specificity (0 - 1). Either a vector of length one listing the point estimate of the diagnostic test specificity or a vector of length three listing (in order) the point estimate, the lower bound of the confidence interval and the upper bound of the confidence interval of the diagnostic test specificity.
lratio.pos	positive likelihood ratio. A vector of length one. Ignored if se and sp are not null.
lratio.neg	negative likelihood ratio. A vector of length one. Ignored if se and sp are not null.
tconf.int	scalar, the magnitude of the confidence interval for the listed diagnostic test performance measures (se and sp).
method	a character string indicating the method used to calculate the confidence intervals for se and sp. Options are method = "exact", method = "wilson", method = "agresti", method = "clopper-pearson" and method = "jeffreys".
verbose	logical, indicating whether detailed or summary results are to be returned.
cred.int	magnitude of the returned credible interval for post-test probability. Must be a single number between 0 and 1.
nsim	scalar, defining the number of simulations to be used for the post-test probability credible interval calculations.

Details

To return a credible interval for the post-test probability this function uses the objective Bayesian method described by Mossman and Berger (2001). In brief, the confidence limits entered by the user for se and sp and specification of the method used to estimate those confidence limits (i.e., method = "exact", method = "wilson", method = "agresti", method = "clopper-pearson" or method = "jeffreys") are used to return the number of study subjects in the study from which the diagnostic test accuracy results were obtained (e.g., the number of individuals outcome and test positive individuals and the number of outcome positive individuals outcome positive for diagnostic sensitivity). Random draws from binomial distributions using shape parameters based on the number of study subjects are then used to generate a distribution of outcome positive post-test probabilities and a distribution of outcome negative post-test probabilities. The setting for credible.int defines the magnitude of the reported credible interval for the post-test probabilities.

Value

A list containing the following:

pretest.ppos	the pre-test probability of being outcome positive, as entered by the user.
pretest.pneg	the pre-test probability of being outcome negative, 1 - pretest.ppos.
postest.ppos	the post-test probability of being outcome positive and the lower and upper bounds of the credible interval of the post-test probability of being outcome positive if confidence limits for se and sp have been provided.
postest.pneg	the post-test probability of being outcome negative and the lower and upper bounds of the credible interval of the post-test probability of being outcome negative if confidence limits for se and sp have been provided.
lratio.pos	the positive likelihood ratio.
lratio.neg	the negative likelihood ratio.

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.

Haskins R, Osmotherly P, Tuyl F, Rivett D, (2014). Uncertainty in clinical prediction rules: The value of credible intervals. Journal of Orthopaedic and Sports Physical Therapy 44: 85 - 91. DOI: 10.2519/jospt.2014.4877.

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

Mossman D, Berger J (2001) Intervals for posttest probabilities: A comparison of 5 methods. Medical Decision Making 21: 498 - 507.

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(pretest.ppos = 0.05, se = 0.890, sp = 0.850,
   lratio.pos = NA, lratio.neg = NA, tconf.int = NA, method = "exact",
   verbose = FALSE, cred.int = 0.95, nsim = 999)

## Given the reference range of 19.0 to 58.0 nmol/L and a test result of
## 22.0 nmol/L we declare this a negative test result.

## If the pre-test probability of being hypothyroid positive is 0.05 and
## the test is negative, the post-test probability of being hypothyroid
## positive is 0.0068.


## EXAMPLE 2:
## A test with diagnostic sensitivity 0.980 (95% CI 0.894 to 0.999) and
## diagnostic specificity 0.980 (95% CI 0.893 to 0.999) has been developed
## to detect feline hepatic lipidosis (FHL). After conducting a  thorough
## clinical examination you are 75% sure that your patient is FHL positive.
## Using the assigned cutpoint for this test, your patient returns a positive
## result. What is the post-test probability that this cat is FHL positive?

epi.nomogram(pretest.ppos = 0.75, se = c(0.980,0.894,0.999),
   sp = c(0.980,0.893,0.999), lratio.pos = NA, lratio.neg = NA,
   tconf.int = 0.95, method = "exact", verbose = FALSE, cred.int = 0.95,
   nsim = 999)

## If the pre-test probability of being FHL positive is 0.75 and the test
## is positive, the post-test probability of being FHL positive is
## 0.99 (95% CrI 0.97 to 1.00).

## If the pre-test probability of being FHL positive is 0.75 and the test
## is negative, the post-test probability of being FHL positive is
## 0.06 (95% CrI 0.0060 to 0.2000). If the cat returns a negative test result
## there's up to a 20% chance that it could still be FHL positive. False
## negatives are a potential problem with this test.
```

`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 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
data.name:	name of the input data, dat.

If pairs = TRUE a list with the following elements. 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}

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

```
## EXAMPLE 1:
## Generate some rating data:

## Not run:
set.seed(1234)
p <- runif(n = 10, min = 0, max = 1)
x <- replicate(n = 5, expr = rbinom(n = 10, size = 4, prob = p) + 1)

rval.occc01 <- epi.occc(dat = x, pairs = TRUE)
print(rval.occc01); summary(rval.occc01)

## End(Not run)
```

---

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

```
## EXAMPLE 1:
dat.v01 <- c(1,1,1,2,2,2,2,3,3,3)
dat.v01 <- as.factor(dat.v01)

dat.ofs01 <- epi.offset(dat.v01)
dat.ofs01
## [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, dilution = FALSE)
```

Arguments

Se	a vector of length one defining the diagnostic sensitivity of the test at the individual sample level.
Sp	a vector of length one defining the diagnostic specificity of the test at the individual sample level.
P	scalar, the expected true prevalence of disease in the group (herd).
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).

dilution	logical. If TRUE the function calculates a value for pooled diagnostic sensitivity dependent on the expected number of positives in the pool. If FALSE pooled diagnostic sensitivity is assumed to be the same as individual sample sensitivity.

Value

A list containing the following:

Se	the diagnostic sensitivity of the test at the individual sample level as entered by the user.
Sp	the diagnostic specificity of the test at the individual sample level as entered by the user.
PlSe	the diagnostic sensitivity of the test when samples are pooled.
PlSp	the diagnostic specificity of the test when samples are pooled.
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 (2014). Veterinary Epidemiologic Research. AVC Inc, Charlottetown, Prince Edward Island, Canada, pp. 126 - 128 .

Christensen J, Gardner IA (2000). Herd-level interpretation of test results for epidemiologic studies of animal diseases. Preventive Veterinary Medicine 45: 83 - 106.

Examples

```
## EXAMPLE 1:
## We want to test dairy herds for Johne's disease using faecal culture
## which has a diagnostic sensitivity and specificity of 0.647 and
## 0.981, respectively. Suppose faecal samples from five cows are pooled
## and we collect six pooled samples per herd. What is the herd level
## sensitivity and specificity using this approach assuming the true prevalence
## of disease is 0.12 and there are no dilution effects arising from pooling.

epi.pooled(Se = 0.647, Sp = 0.981, P = 0.12, m = 5 , r = 6, dilution = FALSE)

## 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.

## Re-calculate herd level sensitivity and specificity assuming there is a
## dilution effect arising from pooling:

epi.pooled(Se = 0.647, Sp = 0.981, P = 0.12, m = 5 , r = 6, dilution = TRUE)

## Herd level sensitivity is 0.943, herd level specificity is 0.562.
```

epi.popsize *Estimate population size on the basis of capture-recapture sampling*

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

```
## EXAMPLE 1:
## 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 to 5557)
## Estimated number of untested pigs: 3240 (95% CI 2365 to 4797)
```

epi.prcc *Partial rank correlation coefficients*

Description

Compute partial rank correlation coefficients.

Usage

```
epi.prcc(dat, sided.test = 2, conf.level = 0.95)
```

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	scalar, 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.
conf.level	magnitude of the returned confidence intervals. Must be a single number between 0 and 1.

Details

Calculation of the PRCC enables the determination of the statistical relationships between each input parameter and the outcome variable while keeping all of the other input parameters constant at their expected value (Conover, 1980). This procedure enables the independent effects of each parameter to be determined, even when the parameters are correlated. A PRCC indicates the degree of monotonicity between a specific input variable and an outcome; therefore only outcome variables that are monotonically related to the input parameters should be chosen for this analysis (Conover, 1980; Iman and Conover 1980). Monotonicity can be assessed by examining scatterplots where each input variable is plotted as a function of the outcome variable. The sign of the PRCC indicates the qualitative relationship between each input variable and the outcome variable. The magnitude of the PRCC indicates the importance of the uncertainty in the input variable in contributing to the imprecision in predicting the value of the outcome variable. The relative importance of the input variables can be directly evaluated by comparing the values of the PRCC.

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 seven elements: var input variable name, est the point estimate of the partial rank corellation coefficient between each input variable and the outcome, lower the lower bound of the confidence interval of the partial rank corellation coefficient, upper the upper bound of the

confidence interval of the partial rank corellation coefficient, `test.statistic` the test statistic used to determine the significance of non-zero values of the partial rank correlation coefficient, `df` the degrees of freedom 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.

Conover WJ (1980). Practical Nonparametric Statistics, 2nd edition, John Wiley and Sons Inc., New York, NY.

Iman RL, Conover WJ (1982). A distribution-free approach to inducing rank correlation among input variables. Communication in Statistics — Simulation and Computation 11: 311 - 334.

Sanchez M, Blower S (1997) Uncertainty and sensitivity analysis of the basic reproductive rate. American Journal of Epidemiology 145: 1127 - 1137.

Examples

```
## EXAMPLE 1:
## Create a matrix of simulation results:
x1 <- rnorm(n = 10, mean = 120, sd = 130)
x2 <- rnorm(n = 10, mean = 80, sd = 5)
x3 <- rnorm(n = 10, mean = 40, sd = 20)
y <- 2 + (0.5 * x1) - (1.7 * x2) + (0.2 * x3)

dat.df01 <- data.frame(x1 = x1, x2 = x2, x3 = x3, y = y)
epi.prcc(dat.df01, sided.test = 2, conf.level = 0.95)
```

---

epi.prev *Estimate true prevalence based on test data and the expected number of false positive and false negative test results*

Description

Compute the true prevalence of a disease and the estimated number of false positive and false negative test results on the basis of an imperfect test. True prevalence can be estimated using either the Rogan Gladen correction or a simplified Bayesian approach.

Usage

```
epi.prev(pos, tested, se, sp, method = "wilson", tp.method = "rogan.gladen",
   bayes.variant = NULL, 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" (Clopper-Pearson), "sterne" (Sterne), "blaker" (Blaker) and "wilson" (Wilson; default).
tp.method	a character string indicating the method used to estimate true prevalence. Options are "rogan.gladen" (Rogan Gladen correction; default) and "simplified.bayes" (simplified Bayesian approach).
bayes.variant	a character string indicating the variant of the simplified Bayesian estimator, used only when tp.method = "simplified.bayes". Options are "mode.hpd" (using the posterior mode as the point estimate and highest posterior density credible intervals) and "median.equaltail" (using the posterior median as the point estimate and equal tail credible intervals). If NULL, "mode.hpd" is used. Ignored when tp.method = "rogan.gladen".
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.

When tp.method = "simplified.bayes", true prevalence is estimated using a simplified Bayesian approach (Kopacka and Fuchs 2026) that accounts for uncertainty in test sensitivity and specificity. Credible intervals are derived from the posterior distribution, using either equal-tailed intervals (posterior median) or highest posterior density (HPD) intervals (posterior mode), depending on bayes.variant. Apparent prevalence and its confidence interval are unaffected and continue to be computed using the method specified by method.

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. For the simplified Bayesian method, intervals reported for true prevalence are Bayesian credible intervals rather than frequentist confidence intervals.
test.positive	the point estimate of the expected number of positive test results and the lower and upper quantiles of the estimated number of positive test results computed using conf.level.
true.positive	the point estimate of the expected number of true positive test results and the lower and upper quantiles of the estimated number of true positive test results computed using conf.level.
false.positive	the point estimate of the expected number of false positive test results and the lower and upper quantiles of the estimated number of false positive test results computed using conf.level.
test.negative	the point estimate of the expected number of negative test results and the lower and upper quantiles of the estimated number of negative test results computed using conf.level.
true.negative	the point estimate of the expected number of true negative test results and the lower and upper quantiles of the estimated number of true negative test results computed using conf.level.
false.negative	the point estimate of the expected number of false negative test results and the lower and upper quantiles of the estimated number of false negative test results computed using conf.level.

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).

If apparent prevalence is less than (1 - diagnostic test specificity) the Rogan Gladen estimate of true prevalence will be less than zero (Speybroeck et al. 2012). If the apparent prevalence is greater than the diagnostic test sensitivity the Rogan Gladen estimate of true prevalence will be greater than one.

When AP < (1 - Sp) the function issues a warning to alert the user that the estimate of true prevalence is invalid. A similar warning is issued when AP > Se. In both situations the estimated number of true positives, false positives, true negatives and false negatives is not returned by the function. Where AP < (1 - Sp) or AP > Se a Bayesian approach for estimation of true prevalence is recommended. See Messam et al. (2008) for a concise introduction to this topic.

Author(s)

Code and documentation for the simplified Bayesian method for this function has been generously provided by Ian Kopacka and Klemens Fuchs, AGES - Osterreichische Agentur fur Gesundheit und Ernahrungssicherheit GmbH, Spargelfeldstrasse 191, 1220 Wien.

References

Abel U (1993). Die Bewertung 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.

Kopacka I, Fuchs K (2026). Overcoming limitations of the Rogan-Gladen correction: A closed-form solution to a simplified Bayesian method for true prevalence estimation. Preventive Veterinary Medicine 253: DOI: 10.1016/j.prevetmed.2026.106891.

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.

Speybroeck N, Devleesschauwer B, Joseph L, Berkvens D (2012). Misclassification errors in prevalence estimation: Bayesian handling with care. International Journal of Public Health DOI:10.1007/s00038-012-0439-9.

Sterne TE (1954). Some remarks on confidence or fiducial limits. Biometrika 41: 275 - 278.

Examples

```
## EXAMPLE 1:
## 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
## 45 were positive to the screening test. What is the estimated prevalence
## of brucellosis in this herd (and its 95% confidence interval)?

epi.prev(pos = 45, 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 22 (95% 14
## to 32) cases per 100 cows at risk. Using this screening test we can expect
## anywhere between 34 and 56 positive test results. Of the positive tests
## between 23 and 42 are expected to be true positives and between 7 and 20 are
## expected to be false positives.


# EXAMPLE 2:
## 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
## -4 (95% CI -6 to 1) cases per 100. The function issues a warning to alert
## the user that estimate of true prevalence invalid. True positive, false
## positive, true negative and false negative counts are not returned. Switch
## tp.method to "simplified.bayes":

epi.prev(pos = 6, tested = 151, se = 0.964, sp = 0.927, method = "c-p",
   tp.method = "simplified.bayes", bayes.variant = "mode.hpd",
   units = 100, conf.level = 0.95)

## The simplified Bayes method allows a valid estimation of true prevalence.
## The estimated true prevalence is 0 (95% CI 0 to 3) cases per 100.


## EXAMPLE 3:
## 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 each of the three herds?

rval.prev03 <- epi.prev(pos = c(80,100,50), 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.prev03$tp, digits = 0)

## True prevalence estimates for each herd:
## Herd 1: 56 (95% CI 43 to 70) cases per 100 cows.
## Herd 2: 80 (95% CI 68 to 92) cases per 100 cows.
## Herd 3: 57 (95% CI 45 to 70) cases per 100 cows.
```

`epi.psi` *Proportional similarity index*

Description

Compute proportional similarity index.

Usage

```
epi.psi(dat, itno = 99, conf.level = 0.95)
```

Arguments

dat	a data frame providing details of the distributions to be compared (in columns). The first column (either a character of factor) lists the levels of each distribution. Additional columns list the number of events for each factor level for each distribution to be compared.
itno	scalar, numeric defining the number of bootstrap simulations to be run to generate a confidence interval around the proportional similarity index estimate.
conf.level	scalar, numeric defining the magnitude of the returned confidence interval for each proportional similarity index estimate.

Details

The proportional similarity or Czekanowski index is an objective and simple measure of the area of intersection between two non-parametric frequency distributions (Feinsinger et al. 1981). PIS values range from 1 for identical frequency distributions to 0 for distributions with no common types. Bootstrap confidence intervals for this measure are estimated based on the approach developed by Garrett et al. (2007).

Value

A five column data frame listing: v1 the name of the reference column, v2 the name of the comparison column, est the estimated proportional similarity index, lower the lower bound of the estimated proportional similarity index, and upper the upper bound of the estimated proportional similarity index.

References

Feinsinger P, Spears EE, Poole RW (1981) A simple measure of niche breadth. Ecology 62: 27 - 32.

Garrett N, Devane M, Hudson J, Nicol C, Ball A, Klena J, Scholes P, Baker M, Gilpin B, Savill M (2007) Statistical comparison of Campylobacter jejuni subtypes from human cases and environmental sources. Journal of Applied Microbiology 103: 2113 - 2121. DOI: 10.1111/j.1365-2672.2007.03437.x.

Mullner P, Collins-Emerson J, Midwinter A, Carter P, Spencer S, van der Logt P, Hathaway S, French NP (2010). Molecular epidemiology of Campylobacter jejuni in a geographically isolated country with a uniquely structured poultry industry. Applied Environmental Microbiology 76: 2145 - 2154. DOI: 10.1128/AEM.00862-09.

Rosef O, Kapperud G, Lauwers S, Gondrosen B (1985) Serotyping of Campylobacter jejuni, Campylobacter coli, and Campylobacter laridis from domestic and wild animals. Applied and Environmental Microbiology, 49: 1507 - 1510.

Examples

```
## EXAMPLE 1:
## A cross-sectional study of Australian thoroughbred race horses was
## carried out. The sampling frame for this study comprised all horses
## registered with Racing Australia in 2017 -- 2018. A random sample of horses
## was selected from the sampling frame and the owners of each horse
```

```
## invited to take part in the study. Counts of source population horses
## and study population horses are provided below. How well did the geographic
## distribution of study population horses match the source population?

state <- c("NSW","VIC","QLD","WA","SA","TAS","NT","Abroad")
srcp <- c(11372,10722,7371,4200,2445,1029,510,101)
stup <- c(622,603,259,105,102,37,22,0)
dat.df01 <- data.frame(state, srcp, stup)

epi.psi(dat.df01, itno = 99, conf.level = 0.95)

## The proportional similarity index for these data was 0.88 (95% CI 0.86 to
## 0.90). We conclude that the distribution of sampled horses by state
## was consistent with the distribution of the source population by state.

## Not run:
## Compare the relative frequencies of the source and study populations
## by state graphically:
library(ggplot2)

dat.df01$psrcp <- dat.df01$srcp / sum(dat.df01$srcp)
dat.df01$pstup <- dat.df01$stup / sum(dat.df01$stup)
dat.df01 <- dat.df01[sort.list(dat.df01$psrcp),]
dat.df01$state <- factor(dat.df01$state, levels = dat.df01$state)

## Data frame for ggplot2:
gdat.df01 <- data.frame(state = rep(dat.df01$state, times = 2),
   pop = c(rep("Source", times = nrow(dat.df01)),
      rep("Study", times = nrow(dat.df01))),
   pfreq = c(dat.df01$psrcp, dat.df01$pstup))
gdat.df01$state <- factor(gdat.df01$state, levels = dat.df01$state)

## Bar chart of relative frequencies by state faceted by population:
ggplot(data = gdat.df01, aes(x = state, y = pfreq)) +
  theme_bw() +
  geom_bar(stat = "identity", position = position_dodge(), color = "grey") +
  facet_grid(~ pop) +
  scale_x_discrete(name = "State") +
  scale_y_continuous(limits = c(0,0.50), name = "Proportion")

## End(Not run)
```

`epi.realrisk` *An R version of the Winton Centre's RealRisk calculator*

Description

A function to return absolute risks from odds, incidence risk and hazard ratios.

Usage

```
epi.realrisk(measure, measure.type, rE0)
```

Arguments

measure	scalar, the numeric estimate of the specified measure of association.
measure.type	character string, detailing the measure of association type. Options are odds.ratio, risk.ratio, hazard.ratio and pct.change (percentage change).
rE0	scalar, the prevalence of the outcome in the exposure negative ('baseline') group. Must be a number between 0 and 1.

Details

For numerous worked examples and analytical details visit the RealRisk web site at the Winton Centre for Risk and Evidence Communication, The University of Cambridge.

Value

A data frame with four elements: measure, the numeric estimate of the measure of association (as entered by the user), measure.type the measure of association type (as entered by the user), rE0 the prevalence of the outcome in the exposure negative ('baseline') group and rE1 the prevalence of the outcome in the exposure positive ('comparison') group.

References

Horby P, Lim W, Emberson J, Mafham M, Bell J, Linsell L, Staplin N, Brightling C, Ustianowski A, Elmahi E, Prudon B, Green C, Felton T, Chadwick D, Rege K, Fegan C, Chappell L, Faust S, Jaki T, Jeffery K, Montgomery A, Rowan K, Juszczak E, Baillie J, Haynes R, Landray M (2021). Dexamethasone in Hospitalized Patients with COVID-19. New England Journal of Medicine 384, 693 - 704.

Parekh T, Pemmasani S, Desai R (2020). Risk of stroke with E-cigarette and combustible cigarette use in young adults. American Journal of Preventive Medicine 58, 446 - 452.

The Winton Centre for Risk and Evidence Communication, The University of Cambridge.

Examples

```
## EXAMPLE 1:
## A cross-sectional study was conducted to determine if 18 to 44 year olds
## who routinely used e-cigarettes were at greater risk of stroke compared
## with individuals of the same age who did not smoke (Parekh et al., 2021).
## The risk of stroke among those 18 to 44 years of age was estimated to
## be 0.6% per year.

## Current dual use of e-cigarettes and combustible cigarettes was associated
## with a 2.91 times higher odds of stroke compared with non-smokers
## (adjusted OR = 2.91, 95% CI 1.62 to 5.25). Report these findings in
## absolute terms.

epi.realrisk(measure = 2.91, measure.type = "odds.ratio", rE0 = 0.006)
```

```
## For those who do not smoke we would expect around 1 in every 100 to suffer
## from stroke. For those who smoke we would expect around 2 in every 100
## to suffer from stroke.


## EXAMPLE 2:
## In a controlled, open-label trial comparing a range of possible treatments
## in patients who were hospitalised with COVID-19 (Horby et al., 2021),
## patients were randomly assigned to receive oral or intravenous
## dexamethasone for up to 10 days or to receive usual care alone. The
## primary outcome for this study was 28-day mortality. The risk of 28-day
## mortality among patients receiving mechanical ventilation and usual care
## was 0.414.

## The risk of death within 28 days of admission among mechanically
## ventilated COVID-19 patients receiving dexamethasone was 0.64
## (95% CI 0.51 to 0.82) times that of mechanically ventilated COVID-19
## patients receiving usual care. Report these findings in absolute terms.

epi.realrisk(measure = c(0.51,0.64,0.82), measure.type = "risk.ratio",
   rE0 = 0.414)

## Out of 100 UK patients receiving mechanical ventilation and
## usual care for COVID-19, we would expect around 41 to die after 28 days.
## Out of 100 UK patients receiving mechanical ventilation and dexamethasone
## for COVID-19, we would expect around 26 (95% CI 21 to 34) to die after
## 28 days.
```

`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.smd` *Fixed-effects 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.smr *Confidence intervals and tests of statistical significance of the standardised mortality [morbidity] ratio*

Description

Computes confidence intervals and tests of statistical significance of the standardised mortality [morbidity] ratio.

Usage

```
epi.smr(obs, exp, method = "byar", conf.level = 0.95)
```

Arguments

obs	scalar integer, defining the observed number of events.
exp	scalar number, defining the expected number of events.
method	character string, defining the method used. Options are chi2, mid.p, fisher, byar, rothman.greenland, ury.wiggins and vandenbroucke. See details, below.
conf.level	magnitude of the returned confidence interval. Must be a single number between 0 and 1.

Details

This function calculates the standardised mortality [morbidity] ratio based on scalars defining the observed and expected number of [disease] events.

The hypothesis that the SMR equals one is tested using the Chi square test, the Mid-P exact test, the Fisher exact test and Byar's approximation. Confidence intervals for the SMR are calculated using the Mid-P exact test, the Fisher exact test, Byar's approximation, Rothman and Greenland's method, Ury and Wiggin's method and the Vandenbroucke method.

Exact confidence intervals and p-values should be used when the number of observed events is less than or equal to five. For greater numbers of observed events, the approximation methods (Byar's, Rothman and Greenland, Ury and Wiggins and Vandenbroucke) should be used.

A two-sided test of significance is returned, using the test statistic appropriate for the method used.

Value

A data frame listing:

obs	the observed number of events, as entered by the user.
exp	the expected number of events, as entered by the user.
est	the point estimate of the SMR.
lower	the lower bound of the confidence interval of the SMR.

upper	the upper bound of the confidence interval of the SMR.
test.statistic	test statistic of the significance of the SMR.
p.value	the probability that the null hypothesis (i.e., the number of observed events divided by the expected number of events equals 1) is true.

Note

Only 90%, 95% and 99% confidence limits are computed using the Ury and Wiggins method. If conf.level does not equal 0.90, 0.95 or 0.99 NAs are returned for the lower and upper bound of the SMR confidence interval.

Only 95% confidence limits are computed using Vandenbroucke's method. If conf.level does not equal 0.95 NAs are returned for the lower and upper bound of the SMR confidence interval.

To calculate SMRs and their confidence intervals for a series of study areas (instead of one) see the epi.conf function using ctype = "smr". To calculate the expected number of events see Example 1 in epi.bohning.

References

Armitage P, Berry G, Mathews J (2002). Statistical Methods in Medical Research. Blackwell Publications London.

Lash TL, VanderWeele TJ, Haneuse S, Rothman KJ (2021). Modern Epidemiology. Lippincott - Raven Philadelphia, USA, pp. 99.

Miettinen OS (1974). Comment. Journal of the American Statistical Association 69: 380 - 382.

Rothman K, Boice J (1979). Epidemiologic Analysis with a Programmable Calculator. U.S. Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health, Washington, USA.

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

Ury H, Wiggins A (1985). Another shortcut method for calculating the confidence interval of a Poisson variable (or of a standardized mortality ratio). American Journal of Epidemiology 122, 197 - 198.

Vandenbroucke J, (1982). A shortcut method for calculating the 95 percent confidence interval of the standardized mortality ratio (Letter). American Journal of Epidemiology 115, 303 - 304.

Examples

```
## EXAMPLE 1:
## The observed number of disease events in a province is 4; the expected
## number of disease events is 3.3. What is the standardised morbidity ratio
## and its 95% confidence interval? Test the hypothesis that the SMR equals
## one.

epi.smr(obs = 4, exp = 3.3, method = "mid.p", conf.level = 0.95)

## The standardised morbidity ratio is 1.2 (95% CI 0.38 to 2.9). We accept
## the null hypothesis and conclude that the SMR does not significantly
## differ from one (p = 0.657).
```

epi.sscc *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.sscc(N = NA, OR, p1 = NA, p0, n, power, r = 1,
   phi.coef = 0, design = 1, sided.test = 2, nfractional = FALSE,
   conf.level = 0.95, method = "unmatched", fleiss = FALSE)
```

Arguments

N	scalar, the total number of subjects eligible for inclusion in the study. If N = NA the eligible population size is assumed to be infinite.
OR	scalar, the expected study odds ratio.
p1	scalar, the prevalence of exposure amongst the cases.
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.
phi.coef	scalar, the correlation between case and control exposures for matched pairs. 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 odds of exposure in controls. Use a one-sided test to evaluate whether or not the odds of exposure in cases is greater than the odds of exposure in controls.
nfractional	logical, return fractional sample size.
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, some of them reproduced below) is provided by Woodward (2014), pp. 295 - 329.

A value for p1 is only required if Fleiss correction is used. For this reason the default for p1 is set to NA.

The correlation between case and control exposures for matched pairs (phi.coef) can be estimated from previous studies using Equation (6.2) from Fleiss et al. 2003, p. 98. In the function epi.2by2 the variable phi.coef is included with the output for each of the uncorrected chi-squared tests. This value can be used for argument phi.coef in epi.sscc.

The methodology described in Woodward (2014), pp. 295 - 329 uses the proportion of discordant pairs to to determine the sample size for a matched case-control study. Note that the proportion of discordant pairs is likely to vary considerably between different studies since it depends not only on the correlation between case and control exposures but also on the exposure prevalence and the odds ratio. In contrast, estimates of phi.coef should be more stable between similar studies.

When no estimate of phi.coef is available, investigators may prefer to perform their power calculations under the assumption that phi.coef equals, say, 0.2 rather than make the questionable independence assumption required by most other methods.

If a value is entered for N a finite population correction factor (Cochran 1977) is applied to the calculated sample size estimate. That is:

$$n_{adj} = \frac{n}{1 + \left(\frac{n}{N}\right)}$$

Power calculations used in this function are based on the uncorrected chi-square (as opposed to Fisher's exact) test.

When nfractional = FALSE the calculated number of cases and controls is rounded up to the next highest integer. The total number of study subjects is then the rounded number of cases plus the rounded number of controls.

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.sscohortc for an example using the design facility implemented in this function.

References

Cochran WG (1977). Sampling Techniques. John Wiley and Sons, London.

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

Fleiss JL, Levin B, Paik MC (2003). Statistical Methods for Rates and Proportions. John Wiley and Sons, New York.

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

Woodward M (2014). Epidemiology Study Design and Data Analysis. Chapman & Hall/CRC, New York, pp. 295 - 329.

Examples

```
## EXAMPLE 1 (from Woodward 2014 Example 8.17 p. 318):
## 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.sscc(N = NA, OR = 2.0, p1 = NA, p0 = 0.30, n = NA, power = 0.90, r = 1,
   phi.coef = 0, design = 1, sided.test = 2, nfractional = FALSE,
   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 2014 Example 8.18 p. 320):
## 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.sscc(N = NA, OR = 2.0, p1 = NA, p0 = 0.30, n = n, power = NA, r = 5,
   phi.coef = 0, design = 1, sided.test = 2, nfractional = FALSE,
   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.sscc(N = NA, OR = 2.0, p1 = NA, p0 = 0.10, n = 600, power = NA, r = 1,
   phi.coef = 0.01, design = 1, sided.test = 2, nfractional = FALSE,
   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.sscc(N = NA, OR = 2.0, p1 = NA, p0 = 0.20, n = NA, power = 0.90, r = 3,
   phi.coef = 0, design = 1, sided.test = 2, nfractional = FALSE,
   conf.level = 0.95, method = "unmatched", fleiss = FALSE)

## A total of 619 subjects need to be enrolled in the study: 155 cases and
## 464 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
## (phi.coef) is estimated to be 0.01 (low). Using the same assumptions as
## those described above, how many study subjects will be required?

epi.sscc(N = NA, OR = 2.0, p1 = NA, p0 = 0.20, n = NA, power = 0.90, r = 1,
   phi.coef = 0.01, design = 1, sided.test = 2, nfractional = FALSE,
   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.df05 <- expand.grid(p0 = p0, OR = OR)
dat.df05$n.total <- NA

for(i in 1:nrow(dat.df05)){
   dat.df05$n.total[i] <- epi.sscc(N = NA, OR = dat.df05$OR[i], p1 = NA,
      p0 = dat.df05$p0[i], n = NA, power = 0.80, r = 1,
      phi.coef = 0, design = 1, sided.test = 2, nfractional = FALSE,
      conf.level = 0.95, method = "unmatched", fleiss = FALSE)$n.total
}

grid.n <- matrix(dat.df05$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)

ggplot(data = dat.df05, aes(x = p0, y = OR, z = n.total)) +
  theme_bw() +
  geom_contour(aes(colour = after_stat(level)), breaks = breaks) +
  scale_x_continuous(limits = c(0, 1),
     name = "Proportion of controls exposed") +
  scale_y_continuous(limits = c(1, 6),
     name = "Minimum OR to detect")

## End(Not run)


## EXAMPLE 6 (from Dupont 1988, p. 1164):
## 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 (phi.coef) 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.sscc(N = NA, OR = 3.0, p1 = NA, p0 = 0.60, n = NA, power = 0.80, r = 1,
   phi.coef = 0.2, design = 1, sided.test = 2, nfractional = FALSE,
   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.sscc(N = NA, OR = 3.0, p1 = NA, p0 = 0.60, n = NA, power = 0.80, r = 3,
   phi.coef = 0.2, design = 1, sided.test = 2, nfractional = FALSE,
   conf.level = 0.95, method = "matched", fleiss = FALSE)

## A total of 203 subjects need to be enrolled in the study: 51 cases and
## 152 controls.
```

`epi.ssclus1estb` *Sample size to estimate a binary outcome using one-stage cluster sampling*

Description

Sample size to estimate a binary outcome using one-stage cluster sampling.

Usage

```
epi.ssclus1estb(N.psu = NA, b, Py, epsilon, error = "relative",
   rho, se, sp, nfractional = FALSE, conf.level = 0.95)
```

Arguments

`N.psu`	scalar integer, the total number of primary sampling units eligible for inclusion in the study. If `N = NA` the eligible primary sampling unit population size is assumed to be infinite.
`b`	scalar integer or vector of length two, the number of individual listing units in each cluster to be sampled. See details, below.
`Py`	scalar number, an estimate of the unknown population proportion.
`epsilon`	scalar number, the maximum difference between the estimate and the unknown population value expressed in absolute or relative terms.
`error`	character string. Options are `absolute` for absolute error and `relative` for relative error.
`rho`	scalar number, the intracluster correlation coefficient.
`se`	the diagnostic sensitivity of the method used to detect positive outcomes (0 - 1).
`sp`	the diagnostic specificity of the method used to detect positive outcomes (0 - 1).
`nfractional`	logical, return fractional sample size.
`conf.level`	scalar, defining the level of confidence in the computed result.

Details

In many situations it is common for sampling units to be aggregated into clusters. Typical examples include individuals within households, children within classes (within schools) and cows within herds. We use the term primary sampling unit (PSU) to refer to what gets sampled first (clusters) and secondary sampling unit (SSU) to refer to what gets sampled second (individual listing units within each cluster). In this documentation the terms primary sampling unit and cluster are used interchangeably. Similarly, the terms secondary sampling unit and individual listing units are used interchangeably.

b as a scalar integer represents the total number of individual listing units from each cluster to be sampled. If b is a vector of length two the first element represents the mean number of individual listing units to be sampled from each cluster and the second element represents the standard deviation of the number of individual listing units to be sampled from each cluster.

At least 25 PSUs (clusters) are recommended for one-stage cluster sampling designs. If less than 25 PSUs are returned by the function a warning is issued.

If a value is entered for N.psu a finite population correction factor (Cochran 1977) is applied to the calculated sample size estimate. That is:

$$n_{adj} = \frac{n}{1 + \left(\frac{n}{N}\right)}$$

Value

A list containing the following:

n.psu	the total number of primary sampling units (clusters) to be sampled for the specified level of confidence and relative error.
n.ssu	the total number of secondary sampling units to be sampled for the specified level of confidence and relative error.
DEF	the design effect.
rho	the intracluster correlation coefficient, as entered by the user.

References

Cochran WG (1977). Sampling Techniques. John Wiley and Sons, London.

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

Machin D, Campbell MJ, Tan SB, Tan SH (2018). Sample Sizes for Clinical, Laboratory ad Epidemiological Studies, Fourth Edition. Wiley Blackwell, London, pp. 195 - 214.

Examples

```
## EXAMPLE 1:
## An aid project has distributed cook stoves in a single province in a
## resource-poor country. At the end of three years, the donors would like
## to know what proportion of households are still using their donated
## stove. A cross-sectional study is planned where villages in the province
## will be sampled and all households (approximately 75 per village) will be
```

```
## visited to determine whether or not the donated stove is still in use.
## A pilot study of the prevalence of stove usage in five villages
## showed that 0.46 of householders were still using their stove. The
## intracluster correlation for a study of this type is unknown, but thought
## to be relatively high (rho = 0.20).

# If the donor wanted to be 90% confident that the survey estimate of stove
## usage was within 10% of the true population value, how many villages
## (i.e., clusters) would need to be sampled?

epi.ssclus1estb(N.psu = NA, b = 75, Py = 0.46, epsilon = 0.10,
   error = "relative", rho = 0.20, se = 1, sp = 1, nfractional = FALSE,
   conf.level = 0.90)

## A total of 67 villages need to be sampled to meet the specifications
## of this study.

## Now imagine the situation where the number of households per village
## varies. We are told that the average number of households per village is
## 75 with the 0.025 quartile 40 households and the 0.975 quartile 180
## households. The expected standard deviation of the number of households
## per village is (180 - 40) / 4 = 35. How many villages need to be sampled?

epi.ssclus1estb(N.psu = NA, b = c(75,35), Py = 0.46, epsilon = 0.10,
   error = "relative", rho = 0.20, se = 1, sp = 1, nfractional = FALSE,
   conf.level = 0.90)

## A total of 81 villages need to be sampled to meet the specifications
## of this study.

## Now imagine the situation where this study is to be carried out on a
## remote island where the total number of villages is 220. Recalculate
## your sample size.

epi.ssclus1estb(N.psu = 220, b = c(75,35), Py = 0.46, epsilon = 0.10,
   error = "relative", rho = 0.20, se = 1, sp = 1, nfractional = FALSE,
   conf.level = 0.90)

## A total of 60 villages need to be sampled to meet the specifications
## of this study.
```

`epi.ssclus1estc` *Sample size to estimate a continuous outcome using one-stage cluster sampling*

Description

Sample size to estimate a continuous outcome using one-stage cluster sampling.

Usage

```
epi.ssclus1estc(N.psu = NA, b, xbar, xsigma, epsilon, error = "relative",
   rho, nfractional = FALSE, conf.level = 0.95)
```

Arguments

N.psu	scalar integer, the total number of primary sampling units eligible for inclusion in the study. If N = NA the eligible primary sampling unit population size is assumed to be infinite.
b	scalar integer or vector of length two, the number of individual listing units in each cluster to be sampled. See details, below.
xbar	scalar number, the expected mean of the continuous variable to be estimated.
xsigma	scalar number, the expected standard deviation of the continuous variable to be estimated.
epsilon	scalar number, the maximum difference between the estimate and the unknown population value expressed in absolute or relative terms.
error	character string. Options are absolute for absolute error and relative for relative error.
rho	scalar number, the intracluster correlation coefficient.
nfractional	logical, return fractional sample size.
conf.level	scalar number, the level of confidence in the computed result.

Details

In many situations it is common for sampling units to be aggregated into clusters. Typical examples include individuals within households, children within classes (within schools) and cows within herds. We use the term primary sampling unit (PSU) to refer to what gets sampled first (clusters) and secondary sampling unit (SSU) to refer to what gets sampled second (individual listing units within each cluster). In this documentation the terms primary sampling unit and cluster are used interchangeably. Similarly, the terms secondary sampling unit and individual listing units are used interchangeably.

b as a scalar integer represents the total number of individual listing units from each cluster to be sampled. If b is a vector of length two the first element represents the mean number of individual listing units to be sampled from each cluster and the second element represents the standard deviation of the number of individual listing units to be sampled from each cluster.

If a value is entered for N.psu a finite population correction factor (Cochran 1977) is applied to the calculated sample size estimate. That is:

$$n_{adj} = \frac{n}{1 + \left(\frac{n}{N}\right)}$$

Value

A list containing the following:

n.psu	the total number of primary sampling units (clusters) to be sampled for the specified level of confidence and relative error.
n.ssu	the total number of secondary sampling units to be sampled for the specified level of confidence and relative error.
DEF	the design effect.
rho	the intracluster correlation coefficient, as entered by the user.

References

Cochran WG (1977). Sampling Techniques. John Wiley and Sons, London.

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

Machin D, Campbell MJ, Tan SB, Tan SH (2018). Sample Sizes for Clinical, Laboratory ad Epidemiological Studies, Fourth Edition. Wiley Blackwell, London, pp. 195 - 214.

Examples

```
## EXAMPLE 1:
## A survey to estimate the average number of residents over 75 years of
## age that require the services of a nurse in a given retirement village is
## to be carried out using a one-stage cluster sampling strategy.
## There are five housing complexes in the village with 25 residents in each.
## We expect that there might be an average of 34 residents meeting this
## criteria (SD 5.5). We would like the estimated sample size to provide us
## with an estimate that is within 10% of the true value. Previous studies
## report an intracluster correlation for the number of residents requiring the
## services of a nurse in this retirement village housing complexes to
## be 0.10. How many housing complexes (clusters) should be sampled?

epi.ssclus1estc(N.psu = NA, b = 25, xbar = 34, xsigma = 5.5,
   epsilon = 0.10, error = "relative", rho = 0.10, nfractional = FALSE,
   conf.level = 0.95)

## A total of 2 housing complexes need to be sampled to meet the specifications
## of this study.
```

---

epi.ssclus2estb *Number of clusters to be sampled to estimate a binary outcome using two-stage cluster sampling*

Description

Number of clusters to be sampled to estimate a binary outcome using two-stage cluster sampling.

Usage

```
epi.ssclus2estb(N.psu = NA, b, Py, epsilon, error = "relative",
   rho, se, sp, nfractional = FALSE, conf.level = 0.95)
```

Arguments

N.psu	scalar integer, the total number of primary sampling units eligible for inclusion in the study. If N = NA the eligible primary sampling unit population size is assumed to be infinite.
b	scalar integer or vector of length two, the number of individual listing units in each cluster to be sampled. See details, below.
Py	scalar number, an estimate of the unknown population proportion.
epsilon	scalar number, the maximum difference between the estimate and the unknown population value expressed in absolute or relative terms.
error	character string. Options are absolute for absolute error and relative for relative error.
rho	scalar number, the intracluster correlation coefficient.
se	the diagnostic sensitivity of the method used to detect positive outcomes (0 - 1).
sp	the diagnostic specificity of the method used to detect positive outcomes (0 - 1).
nfractional	logical, return fractional sample size.
conf.level	scalar, defining the level of confidence in the computed result.

Details

In many situations it is common for sampling units to be aggregated into clusters. Typical examples include individuals within households, children within classes (within schools) and cows within herds. We use the term primary sampling unit (PSU) to refer to what gets sampled first (clusters) and secondary sampling unit (SSU) to refer to what gets sampled second (individual listing units within each cluster). In this documentation the terms primary sampling unit and cluster are used interchangeably. Similarly, the terms secondary sampling unit and individual listing units are used interchangeably.

b as a scalar integer represents the total number of individual listing units from each cluster to be sampled. If b is a vector of length two the first element represents the mean number of individual listing units to be sampled from each cluster and the second element represents the standard deviation of the number of individual listing units to be sampled from each cluster.

The methodology used in this function follows the approach described by Bennett et al. (1991). At least 25 PSUs are recommended for two-stage cluster sampling designs. If less than 25 PSUs are returned by the function a warning is issued.

As a rule of thumb, around 30 PSUs will provide good estimates of the true population value with an acceptable level of precision (Binkin et al. 1992) when: (1) the true population value is between 10% and 90%; and (2) the desired absolute error is around 5%. For a fixed number of individual listing units selected per cluster (e.g., 10 individuals per cluster or 30 individuals per cluster), collecting information on more than 30 clusters can improve the precision of the final population estimate, however, beyond around 60 clusters the improvement in precision is minimal.

If a value is entered for N.psu a finite population correction factor (Cochran 1977) is applied to the calculated sample size estimate. That is:

$$n_{adj} = \frac{n}{1 + \left(\frac{n}{N}\right)}$$

Value

A list containing the following:

n.psu	the total number of primary sampling units (clusters) to be sampled for the specified level of confidence and relative error.
n.ssu	the total number of secondary sampling units to be sampled for the specified level of confidence and relative error.
DEF	the design effect.
rho	the intracluster correlation coefficient, as entered by the user.

References

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

Binkin N, Sullivan K, Staehling N, Nieburg P (1992). Rapid nutrition surveys: How many clusters are enough? Disasters 16: 97 - 103.

Cochran WG (1977). Sampling Techniques. John Wiley and Sons, London.

Machin D, Campbell MJ, Tan SB, Tan SH (2018). Sample Sizes for Clinical, Laboratory ad Epidemiological Studies, Fourth Edition. Wiley Blackwell, London, pp. 195 - 214.

Examples

```
## EXAMPLE 1 (from Bennett et al. 1991 p 102):
## We intend to conduct a cross-sectional study to determine the prevalence
## of disease X in a given country. The expected prevalence of disease is
## thought to be around 20%. Previous studies report an intracluster
## correlation coefficient for this disease to be 0.02. Suppose that we want
## to be 95% certain that our estimate of the prevalence of disease is
## within 5% of the true population value and that we intend to sample 20
## individuals per cluster. The diagnostic test we're using has a sensitivity
## of 0.92 and specificity of 0.96. How many clusters should be sampled to meet
## the requirements of the study?

epi.ssclus2estb(N.psu = NA, b = 20, Py = 0.20, epsilon = 0.05,
   error = "absolute", rho = 0.02, se = 0.92, sp = 0.96, nfractional = FALSE,
   conf.level = 0.95)

## A total of 24 clusters need to be sampled to meet the specifications
## of this study. epi.ssclus2estb returns a warning message that the number of
## clusters is less than 25.
```

---

epi.ssclus2estc *Number of clusters to be sampled to estimate a continuous outcome using two-stage cluster sampling*

Description

Number of clusters to be sampled to estimate a continuous outcome using two-stage cluster sampling.

Usage

```
epi.ssclus2estc(N.psu, N.ssu, b, xbar, xsigma, epsilon, error = "relative",
   rho, nfractional = FALSE, conf.level = 0.95)
```

Arguments

N.psu	scalar integer, the total number of primary sampling units eligible for inclusion in the study. If N = NA the eligible primary sampling unit population size is assumed to be infinite.
N.ssu	scalar integer, the total number of secondary sampling units eligible for inclusion in the study.
b	scalar integer or vector of length two, the number of individual listing units in each cluster to be sampled. See details, below.
xbar	scalar number, the expected mean of the continuous variable to be estimated.
xsigma	scalar number, the expected standard deviation of the continuous variable to be estimated.
epsilon	scalar number, the maximum difference between the estimate and the unknown population value expressed in absolute or relative terms.
error	character string. Options are absolute for absolute error and relative for relative error.
rho	scalar number, the intracluster correlation coefficient.
nfractional	logical, return fractional sample size.
conf.level	scalar number, the level of confidence in the computed result.

Details

In many situations it is common for sampling units to be aggregated into clusters. Typical examples include individuals within households, children within classes (within schools) and cows within herds. We use the term primary sampling unit (PSU) to refer to what gets sampled first (clusters) and secondary sampling unit (SSU) to refer to what gets sampled second (individual listing units within each cluster). In this documentation the terms primary sampling unit and cluster are used interchangeably. Similarly, the terms secondary sampling unit and individual listing units are used interchangeably.

b as a scalar integer represents the total number of individual listing units from each cluster to be sampled. If b is a vector of length two the first element represents the mean number of individual listing units to be sampled from each cluster and the second element represents the standard deviation of the number of individual listing units to be sampled from each cluster.

If a value is entered for N.psu a finite population correction factor (Cochran 1977) is applied to the calculated sample size estimate. That is:

$$n_{adj} = \frac{n}{1 + \left(\frac{n}{N}\right)}$$

Value

A list containing the following:

n.psu	the total number of primary sampling units (clusters) to be sampled for the specified level of confidence and relative error.
n.ssu	the total number of secondary sampling units to be sampled for the specified level of confidence and relative error.
DEF	the design effect.
rho	the intracluster correlation coefficient, as entered by the user.

References

Cochran WG (1977). Sampling Techniques. John Wiley and Sons, London.

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

Machin D, Campbell MJ, Tan SB, Tan SH (2018). Sample Sizes for Clinical, Laboratory ad Epidemiological Studies, Fourth Edition. Wiley Blackwell, London, pp. 195 - 214.

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). Previous studies report an intracluster
## correlation for the number of patients seen per nurse to be 0.02.
## How many health centres should be sampled?

epi.ssclus2estc(N.psu = 5, N.ssu = 15, b = 2, xbar = 28, xsigma = sqrt(160),
   epsilon = 0.30, error = "relative", rho = 0.02, nfractional = FALSE,
   conf.level = 0.95)

## A total of 3 health centres need to be sampled to meet the specifications
## of this study.
```

---

epi.sscohortc *Sample size, power or minimum detectable incidence risk ratio for a cohort study using individual count data*

Description

Sample size, power or minimum detectable incidence risk ratio for a cohort study using individual count data.

Usage

```
epi.sscohortc(N = NA, irexp1, irexp0, pexp = NA, n, power, r = 1,
   design = 1, sided.test = 2, finite.correction = FALSE,
   nfractional = FALSE, conf.level = 0.95)
```

Arguments

N	scalar integer, the total number of individuals eligible for inclusion in the study. If N = NA the number of individuals eligible for inclusion is assumed to be infinite.
irexp1	the expected incidence risk of the outcome in the exposed group (0 to 1).
irexp0	the expected incidence risk of the outcome in the non-exposed group (0 to 1).
pexp	the expected prevalence of exposure to the hypothesised risk factor in the population (0 to 1).
n	scalar, defining the total number of subjects in the study (i.e., the number in both the exposed and unexposed groups).
power	scalar, the required study power.
r	scalar, the number in the exposed group divided by the number in the unexposed 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 outcome incidence risk in the exposed group is greater than or less than the outcome incidence risk in the unexposed group. Use a one-sided test to evaluate whether or not the outcome incidence risk in the exposed group is greater than the outcome incidence risk in the unexposed group.
finite.correction	logical, apply a finite correction factor?
nfractional	logical, return fractional sample size.
conf.level	scalar, defining the level of confidence in the computed result.

Details

The methodology in this function follows the methodology described in Chapter 8 of Woodward (2014), pp. 295 - 329.

If a value is entered for N.psu a finite population correction factor (Cochran 1977) is applied to the calculated sample size estimate. That is:

$$n_{adj} = \frac{n}{1 + \left(\frac{n}{N}\right)}$$

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 exposed (treatment) group compared with the non-exposed (control) group.
n.exp1	the total number of subjects in the exposed (treatment) group for the specified level of confidence and power, respecting the requirement for r times as many individuals in the exposed (treatment) group compared with the non-exposed (control) group.
n.exp0	the total number of subjects in the non-exposed (control) group for the specified level of confidence and power, respecting the requirement for r times as many individuals in the exposed (treatment) group compared with the non-exposed (control) group.
power	the power of the study given the number of study subjects, the expected effect size and level of confidence.
irr	the incidence risk of the outcome in the exposed group divided by the incidence risk of the outcome in the unexposed group (the incidence risk ratio).
or	the odds of the outcome in the exposed group divided by the odds of the outcome in the unexposed group (the odds 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 irexp0, pexp, n, and power to return a value for irr. In this situation, the lower value of irr represents the maximum detectable incidence risk ratio that is less than 1; the upper value of irr represents the minimum detectable incidence risk ratio greater than 1. A value for pexp doesn't need to be entered if you want to calculate sample size or study power.

When calculating study power or minimum detectable incidence risk ratio when finite.correction = TRUE the function takes the values of n and N entered by the user and back-calculates a value of n assuming an infinite population. Values for power, irr and or are then returned, assuming the back-calculated value of n is equivalent to the value of n entered by the user.

References

Cochran WG (1977). Sampling Techniques. John Wiley and Sons, London.

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

Woodward M (2014). Epidemiology Study Design and Data Analysis. Chapman & Hall/CRC, New York, pp. 295 - 329.

Examples

```
## EXAMPLE 1 (from Woodward 2014 Example 8.13 p. 314):
## 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 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?

irexp1 = 1.4 * (5 * 413) / 100000; irexp0 = (5 * 413) / 100000
epi.sscohortc(N = NA, irexp1 = irexp1, irexp0 = irexp0, pexp = NA, n = NA,
   power = 0.90, r = 1, design = 1, sided.test = 1,
   finite.correction = FALSE, nfractional = FALSE, conf.level = 0.95)

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


## EXAMPLE 2:
## 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?

irexp0 = (5 * 413)/100000
epi.sscohortc(N = NA, irexp1 = NA, irexp0 = irexp0, pexp = NA, n = 5000,
   power = 0.90, r = 1, design = 1, sided.test = 1,
   finite.correction = FALSE, nfractional = FALSE, 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.sscohortc(N = NA, irexp1 = 0.30, irexp0 = 0.15, pexp = NA, n = NA,
   power = 0.80, r = 1, design = 1, sided.test = 2,
   finite.correction = FALSE, nfractional = FALSE, 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 intracluster 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; design
```

```
## The design effect is 2.45.

epi.sscohortc(N = NA, irexp1 = 0.30, irexp0 = 0.15, pexp = NA, n = NA,
   power = 0.80, r = 1, design = design, sided.test = 2,
   finite.correction = FALSE, nfractional = FALSE, 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.sscohortt` *Sample size, power or minimum detectable incidence rate ratio for a cohort study using person or animal time data*

Description

Sample size, power or minimum detectable incidence rate ratio for a cohort study using person or animal time data.

Usage

```
epi.sscohortt(FT = NA, irexp1, irexp0, n, power, r = 1, design = 1,
   sided.test = 2, nfractional = FALSE, conf.level = 0.95)
```

Arguments

`FT`	scalar integer, the follow-up period for the study. If `FT = NA` the follow-up period is assumed to be infinite.
`irexp1`	the expected incidence rate of the outcome in the exposed group (0 to 1).
`irexp0`	the expected incidence rate of the outcome in the non-exposed group (0 to 1).
`n`	scalar, defining the total number of subjects in the study (i.e., the number in both the exposed and unexposed groups).
`power`	scalar, the required study power.
`r`	scalar, the number in the exposed group divided by the number in the unexposed 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 outcome incidence rate in the exposed group is greater than or less than the outcome incidence rate in the unexposed group. Use a one-sided test to evaluate whether or not the outcome incidence rate in the exposed group is greater than the outcome incidence rate in the unexposed group.
`nfractional`	logical, return fractional sample size.
`conf.level`	scalar, defining the level of confidence in the computed result.

Details

The methodology in this function follows the methodology described in Lwanga and Lemeshow (1991).

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.exp1	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.exp0	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.
irr	the incidence rate of the outcome in the exposed group divided by the incidence rate in the unexposed group (the incidence rate 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 irexp0, n, and power to return a value for irr. In this situation, the lower value of irr represents the maximum detectable incidence rate ratio that is less than 1; the upper value of irr represents the minimum detectable incidence rate ratio greater than 1.

See the documentation for epi.sscohortc for an example using the design facility implemented in this function.

References

Lemeshow S, Hosmer D, Klar J, Lwanga S (1990). Adequacy of Sample Size in Health Studies. John Wiley and Sons, New York.

Lwanga S, Lemeshow S (1991). Sample Size Determination in Health Studies. World Health Organization, Geneva.

Examples

```
## EXAMPLE 1 (from Lwanga and Lemeshow 1991 p. 19):
## As part of a study of the long-term effect of noise on workers in a
## particularly noisy industry, it is planned to follow up a cohort of people
## who were recruited into the industry during a given period of time and to
## compare them with a similar cohort of individuals working in a much
## quieter industry. Subjects will be followed up for the rest of their lives or
```

```
## until their hearing is impaired. The results of a previous small-scale survey
## suggest that the annual incidence rate of hearing impairment in the noisy
## industry may be as high as 25%. How many people should be followed up
## in each of the groups (which are to be of equal size) to test the hypothesis
## that the incidence rates for hearing impairment in the two groups are the
## same, at the 5% level of significance and with a power of 80%? The
## alternative hypothesis is that the annual incidence rate for hearing
## impairment in the quieter industry is not more than the national average of
## about 10% (for people in the same age range), whereas in the noisy
## industry it differs from this.

## An annuual incidence rate of 25% is equivalent to 25 cases of hearing
## impairment per 100 individuals per year.

epi.sscohortt(FT = NA, irexp1 = 0.25, irexp0 = 0.10, n = NA, power = 0.80,
   r = 1, design = 1, sided.test = 2, nfractional = FALSE, conf.level = 0.95)

## A total of 46 subjects are required for this study: 23 in the exposed
## group and 23 in the unexposed group.


## EXAMPLE 2 (from Lwanga and Lemeshow 1991 p. 19):
## A study similar to that described above is to be undertaken, but the
## duration of the study will be limited to 5 years. How many subjects should
## be followed up in each group?

epi.sscohortt(FT = 5, irexp1 = 0.25, irexp0 = 0.10, n = NA, power = 0.80,
   r = 1, design = 1, sided.test = 2, nfractional = FALSE, conf.level = 0.95)

## A total of 130 subjects are required for this study: 65 in the exposed
## group and 65 in the unexposed group.
```

`epi.sscompb` *Sample size and power when comparing binary outcomes*

Description

Sample size and power when comparing binary outcomes.

Usage

```
epi.sscompb(N = NA, treat, control, n, power, r = 1, design = 1,
   sided.test = 2, nfractional = FALSE, conf.level = 0.95)
```

Arguments

N	scalar integer, the total number of individuals eligible for inclusion in the study. If N = NA the number of individuals eligible for inclusion is assumed to be infinite.

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 outcome proportion in the exposed (treatment) group is greater than or less than the outcome proportion in the unexposed (control) group. Use a one-sided test to evaluate whether or not the outcome proportion in the exposed (treatment) group is greater than the outcome proportion in the unexposed (control) group.
nfractional	logical, return fractional sample size.
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 (2014), pp. 295 - 329.

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.sscohortc 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.sscohortc returns much larger sample size estimates. This function (epi.sscompb) 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.

If a value is entered for N.psu a finite population correction factor (Cochran 1977) is applied to the calculated sample size estimate. That is:

$$n_{adj} = \frac{n}{1 + \left(\frac{n}{N}\right)}$$

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.

See the documentation for epi.sscohortc for an example using the design facility implemented in this function.

References

Cochran WG (1977). Sampling Techniques. John Wiley and Sons, London.

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 (2014). Epidemiology Study Design and Data Analysis. Chapman & Hall/CRC, New York, pp. 295 - 329.

Examples

```
## EXAMPLE 1 (from Woodward 2014 Example 8.12 p. 312):
## 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.sscompb(N = NA, treat = 0.30, control = 0.32, n = NA, power = 0.90,
   r = 1, design = 1, sided.test = 1, nfractional = FALSE, conf.level = 0.95)

## A total of 4568 men should be sampled: 2284 in the treatment group and
## 2284 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 2000 men (1000 in the treatment group and 1000 in the
## control group) what is the maximum detectable risk ratio that is less
```

```
## than 1?

epi.sscompb(N = NA, treat = NA, control = 0.32, n = 2000, power = 0.90,
   r = 1, design = 1, sided.test = 1, nfractional = FALSE, conf.level = 0.95)

## If we sample only 2,000 men the maximum detectable risk ratio will be 0.91.
```

`epi.sscompc` *Sample size and power when comparing continuous outcomes*

Description

Sample size and power when comparing continuous outcomes.

Usage

```
epi.sscompc(N = NA, treat, control, sigma, n, power, r = 1, design = 1,
   sided.test = 2, nfractional = FALSE, conf.level = 0.95)
```

Arguments

`N`	scalar integer, the total number of individuals eligible for inclusion in the study. If `N = NA` the number of individuals eligible for inclusion is assumed to be infinite.
`treat`	the expected value for the treatment group (see below).
`control`	the expected value for the control group (see below).
`sigma`	the expected standard deviation of the variable of interest for both treatment and control groups.
`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.
`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 outcome in the exposed (treatment) group is greater than or less than the outcome in the unexposed (control) group. Use a one-sided test to evaluate whether or not the outcome in the exposed (treatment) group is greater than the outcome in the unexposed (control) group.
`nfractional`	logical, return fractional sample size.
`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 (2014), pp. 295 - 329.

If a value is entered for `N.psu` a finite population correction factor (Cochran 1977) is applied to the calculated sample size estimate. That is:

$$n_{adj} = \frac{n}{1 + \left(\frac{n}{N}\right)}$$

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 (2014), pages 295 to 329.

See the documentation for `epi.sscohortc` for an example using the `design` facility implemented in this function.

References

Cochran WG (1977). Sampling Techniques. John Wiley and Sons, London.

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

Woodward M (1999). Epidemiology Study Design and Data Analysis. Chapman & Hall/CRC, New York, pp. 329 - 365.

Woodward M (2014). Epidemiology Study Design and Data Analysis. Chapman & Hall/CRC, New York, pp. 295 - 329.

Examples

```
## EXAMPLE 1 (from Woodward 2014 Example 8.8 p. 308):
## 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.sscompc(N = NA, treat = 5.0, control = 4.5, sigma = 1.4, n = NA,
   power = 0.95, r = 1, design = 1, sided.test = 1, nfractional = FALSE,
   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 1999 Example 8.9 pp. 345):
## 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 want 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 estimate of its effect.
## How many women should be enrolled in this study?

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

## The estimated sample size is 67. We allocate 70/5 = 14 women to the
## placebo group and four times as many (n = 53) to the iron treatment group.
```

---

epi.sscomps *Sample size and power when comparing time to event*

Description

Sample size and power when comparing time to event.

Usage

```
epi.sscomps(treat, control, n, power, r = 1, design = 1,
   sided.test = 2, nfractional = FALSE, 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 outcome hazard in the exposed (treatment) group is greater than or less than the outcome hazard in the unexposed (control) group. Use a one-sided test to evaluate whether or not the outcome hazard in the exposed (treatment) group is greater than the outcome hazard in the unexposed (control) group.
nfractional	logical, return fractional sample size.
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 events required for the specified level of confidence and power.
n.total	the total estimated number of events required for the specified level of confidence and power, respecting the requirement for r times as many events 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 events, 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.

See the documentation for epi.sscohortc for an example using the design facility implemented in this function.

References

Therneau TM, Grambsch PM (2000). Modelling Survival Data - Extending the Cox Model. Springer, London, pp. 61 - 65.

Woodward M (2014). Epidemiology Study Design and Data Analysis. Chapman & Hall/CRC, New York, pp. 295 - 329.

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.sscomps(treat = 0.45, control = 0.30, n = NA, power = 0.90,
   r = 1, design = 1, sided.test = 2, nfractional = FALSE, 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.sscomps(treat = NA, control = NA, n = 500, power = 0.90,
   r = 1, design = 1, sided.test = 2, nfractional = FALSE, 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.ssdetect *Sample size to detect an event*

Description

Sample size to detect at least one event (e.g., a disease-positive individual) in a population. The method adjusts sample size estimates on the basis of test sensitivity and can account for series and parallel test interpretation.

Usage

```
epi.ssdetect(N, pstar, se, sp, interpretation = "series",
   covar = c(0,0), nfractional = FALSE, se.psu = 0.95, ss.se = 0.95)
```

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 primary sampling units (PSUs, clusters), the second element defining the number of secondary sampling (SSUs) per PSU. Use NA if either of these two values are unknown.
pstar	a vector of length one or two defining the design prevalence. The first element defines the PSU design prevalence. The second element defines the SSU design prevalence.
se	a vector of length one or two defining the sensitivity of the diagnostic test(s) used at the surveillance unit level.
sp	a vector of length one or two defining the specificity of the diagnostic test(s) used at the surveillance unit level.
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 units. The second element of the vector is the covariance between test results for disease negative units. Use covar = c(0,0) (the default) if these values are not known.
nfractional	logical, return fractional sample size.
se.psu	scalar, defining the desired PSU sensitivity of detection. Ignored if N is a vector of length one.
ss.se	scalar, defining the required surveillance system sensitivity.

Value

A list containing the following:

performance	The sensitivity and specificity of the testing strategy.
sample.size	The required number of primary sampling units, secondary sampling units per primary sampling unit, and the total number of secondary sampling units.

Note

If population size estimates are unknown the binomial distribution is used. If population size estimates are known an approximation of the hypergeometric distribution (MacDiarmid 1988).

If the calculated number of PSUs is greater than the listed number of PSUs the function returns the listed number of PSUs as the number of PSUs to sample.

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

Cannon RM (2001). Sense and sensitivity — designing surveys based on an imperfect test. Preventive Veterinary Medicine 49: 141 - 163.

Dohoo I, Martin W, Stryhn H (2009). Veterinary Epidemiologic Research. AVC Inc, Charlottetown, Prince Edward Island, Canada, pp. 54.

MacDiarmid S (1988). Future options for brucellosis surveillance in New Zealand beef herds. New Zealand Veterinary Journal 36, 39 - 42. DOI: 10.1080/00480169.1988.35472.

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 1.00. How many samples should we take to be 95% certain
## that, if all tests are negative, the disease is not present?

epi.ssdetect(N = 1000, pstar = 0.05, se = 0.90, sp = 1.00,
   interpretation = "series", covar = c(0,0),
   nfractional = FALSE, se.psu = 0.95, ss.se = 0.95)

## We need to sample 62 cows.


## EXAMPLE 2:
## We would like to confirm the absence of disease in a study area. If the
## disease is present we expect the prevalence of disease-positive herds to
## 8% and the within-herd prevalence (for disease-positive herds) 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.ssdetect(N = c(5000,100), pstar = c(0.08,0.05), se = c(0.90,0.95),
   sp = c(0.80,0.85), interpretation = "parallel",
   covar = c(0,0), nfractional = FALSE, se.psu = 0.95, ss.se = 0.95)

## We need to sample 46 cows from 40 herds (a total of 1840 samples).
## The sensitivity of this testing regime at the surveillance unit level
## is 0.995. The specificity of this testing regime at the surveillance unit
## level is 0.680.
```

```
## 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.ssdetect(N = 200, pstar = 0.20, se = 0.95, sp = 1,
   interpretation = "parallel", covar = c(0,0), nfractional = FALSE,
   se.psu = 0.95, ss.se = 0.95)

## If you test 16 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.ssdxsesp` *Sample size to estimate the sensitivity or specificity of a diagnostic test*

Description

Sample size to estimate the sensitivity or specificity of a diagnostic test.

Usage

```
epi.ssdxsesp(se, sp, Py, epsilon, error = "relative",
   nfractional = FALSE, conf.level = 0.95)
```

Arguments

`se`	scalar number, the prior estimate of diagnostic test sensitivity (0 to 1).
`sp`	scalar number, the prior estimate of diagnostic test specificity (0 to 1).
`Py`	scalar number, an estimate of the prevalence of the outcome in the study population.
`epsilon`	scalar number, the maximum difference between the estimate and the unknown population value expressed in absolute or relative terms.
`error`	character string. Options are `absolute` for absolute error and `relative` for relative error.
`nfractional`	logical, return fractional sample size.
`conf.level`	scalar number, the level of confidence in the computed result.

Value

A data frame listing: `se`, the prior estimate of diagnostic senstivity as entered by the user, `sp`, the prior estimate of diagnostic specificity as entered by the user, `Py` the estimate of the prevalence of the outcome in the population as entered by the user, `se.n` the sample size to estimate diagnostic sensitivity, `sp.n` the sample size to estimate diagnostic specificity and `total.n` the total sample size for the study (which is the maximum of `se.n` and `sp.n`).

Note

The sample size calculation method implemented in this function follows the approach described by Buderer (1996) and Hajian-Tilaki (2014).

References

Buderer, NM (1996). Statistical methodology: I. Incorporating the prevalence of disease into the sample size calculation for sensitivity and specificity. Academic Emergency Medicine, 3: 895 - 900. DOI: 10.1111/j.1553-2712.1996.tb03538.x

Hajian-Tilaki K (2014). Sample size estimation in diagnostic test studies of biomedical informatics. Journal of Biomedical Informatics 48: 193 - 204. DOI: 10.1016/j.jbi.2014.02.013.

van Hal S, Lahra M, Whiley D (2025) Determining targets for ceftriaxone resistance detection in Neisseria gonorrhoeae based on genotype-phenotype data: An observational study. Lancet Microbe: 101199. DOI: 10.1016/j.lanmic.2025.101199.

Examples

```
## EXAMPLE 1 (from Hajian-Tilaki 2014, p 195):
## A new diagnostic test has been developed and we'd like to conduct a study
## to determine its diagnostic sensitivity which we believe should be in the
## order of 0.80. How many subjects should be enrolled if the prevalence of
## the disease outcome of interest is 0.10 and we'd like to be 95% confident
## that our estimate of sensitivity is within 0.07 of the true population
## value? For this example we want to estimate diagnostic sensitivity (only)
## so the estimated performance measure for specificity is set to NA.

epi.ssdxsesp(se = 0.80, sp = NA, Py = 0.10, epsilon = 0.07,
   error = "absolute", nfractional = FALSE, conf.level = 0.95)

## A total of 1255 subjects need to be enrolled to meet the requirements of the
## study.


## EXAMPLE 2 (from van Hal et al. 2025):
## van Hal et al (2025) determined targets for ceftriaxone resistance detection
## in Neisseria gonorrhoeae based on genotype-phenotype. To estimate
## diagnostic testing performance with high precision [sic], a sample size
## of 8295 distinct MIC-geonotype pairings was required, to achieve a
## sensitivity and specificity of 95%, based on a ceftriaxone resistance
## prevalence of 0.22% --- a value reflecting current rates in high-income
## settings with robust surveillance systems.

## Code to reproduce the sample size calculations reported in the van Hal
## et al. (2025) paper as follows:

epi.ssdxsesp(se = 0.95, sp = 0.95, Py = 0.0022, epsilon = 0.10,
   error = "absolute", nfractional = FALSE, conf.level = 0.95)
```

`epi.ssdxtest` *Sample size to validate a diagnostic test in the absence of a gold standard*

Description

Sample size to validate a diagnostic test in the absence of a gold standard.

Usage

```
epi.ssdxtest(pi, se, sp, epsilon.api, epsilon.ase, epsilon.asp, epsilon.asesp,
    r = 1, nfractional = FALSE, verbose = FALSE, conf.level = 0.95)
```

Arguments

`pi`	vector of length two, the expected prevalence of the outcome of interest in the two populations (0 to 1), respectively.
`se`	vector of length two, the expected diagnostic sensitivity of the first and second test (0 to 1), respectively.
`sp`	vector of length two, the expected diagnostic specificity of the first and second test (0 to 1), respectively.
`epsilon.api`	vector of length two, the absolute error for the prevalence of the outcome of interest in the first and second study populations.
`epsilon.ase`	vector of length two, the absolute error for the sensitivity estimate of the first and second test.
`epsilon.asp`	vector of length two, the absolute error for the specificity estimate of the first and second test.
`epsilon.asesp`	vector of length two, the absolute error for the difference in the two sensitivity and specificity estimates.
`r`	scalar, the required number in the second population divided by the number in the first population.
`nfractional`	logical, return fractional sample size.
`verbose`	logical, return sample size estimates for `se`, `sp`, and `pi`?
`conf.level`	scalar, defining the level of confidence in the computed result.

Details

Hui and Walter (1980) describe an approach for estimating the sensitivity and specificity of a diagnostic test in the absence of a gold standard. Their method involves testing individuals from two populations with two conditionally independent diagnostic tests (neither of which is a gold standard). With such data, all six parameters of interest (two sensitivities, two specificities and two prevalences) can be estimated since there are six degrees of freedom available. The methodology in this function follows the sample size calculation methods described by Georgiadis et al. (2005).

In their paper Georgiadis et al. (2005) parameterise the uncertainty in the prevalence, sensitivity and specificity estimates in terms of the width of the confidence interval. For consistency with the other sample size calculation functions in **epiR** the amount of uncertainty in the prevalence, sensitivity and specificity is parameterised in absolute terms. Using this approach, if we set `se = c(0.80,0.90)` and `epsilon.ase = c(0.05,0.10)` the number of subjects to return an estimate of `se1` that is between `0.75` and `0.85` and `se2` that is between `0.80` and `1.0` will be returned.

Value

When `verbose = TRUE` a data frame listing the required sample size to estimate:

`p1`	the prevalence of the outcome of interest in population 1.
`p2`	the prevalence of the outcome of interest in population 2.
`se1`	the sensitivity of the first diagnostic test.
`se2`	the sensitivity of the second diagnostic test.
`sp1`	the specificity of the first diagnostic test.
`sp2`	the specificity of the second diagnostic test.
`se1.se2`	the difference in the sensitivities of the two diagnostic tests.
`sp1.sp2`	the difference in the specificities of the two diagnostic tests.

When `verbose = FALSE` a data frame listing the maximum of the sample size estimates listed when `verbose = TRUE`.

References

Georgiadis M, Johnson W, Gardner I (2005) Sample size determination for estimation of the accuracy of two conditionally independent tests in the absence of a gold standard. Preventive Veterinary Medicine 71, 1 - 10. DOI: 10.1016/j.prevetmed.2005.04.004.

Hui SL, Walter SD (1980) Estimating the error rates of diagnostic tests. Biometrics 36, 167 - 171.

Nielsen SS, Gronbaek C, Agger JF, Houe H (2002) Maximum-likelihood estimation of sensitivity and specificity of ELISAs and faecal culture for diagnosis of paratuberculosis. Preventive Veterinary Medicine 53, 191 - 204. DOI: 10.1016/s0167-5877(01)00280-x.

Examples

```
## EXAMPLE 1 (from Georgiadis et al. 2005, pp. 5):
## Nielsen et al. (2002) present data from the evaluation of a milk
## antibody ELISA and faecal culture for the diagnosis of Mycobacterium avium
## subsp. paratuberculosis infection in cattle. Because the ELISA detects
## antibodies and culture is based on isolation of the bacterium in faeces
## we can reasonably assume that the two tests are conditionally independent.

## How many cattle need to be sampled if we wanted to be 95% certain that
## our estimate of diagnostic sensitivity and specificity of the two tests
## is within 0.05 of the true population value assuming the number sampled
## in the second population divided by the number sampled in the first
## population is 0.817? The prevalence of Mycobacterium avium subsp.
## paratuberculosis is thought to be 0.093 and 0.204, respectively. Assume
```

```
## the sensitivity of the the ELISA and faecal culture is 0.349 and 0.534,
## respectively. Assume the specificity of the ELISA and faecal culture is
## 0.995 and 0.894, respectively.

epi.ssdxtest(pi = c(0.093,0.204), se = c(0.349,0.534), sp = c(0.995,0.894),
   epsilon.api = c(0.05,0.05), epsilon.ase = c(0.05,0.05),
   epsilon.asp = c(0.05,0.05), epsilon.asesp = c(0.05,0.05),
    r = 0.817, nfractional = FALSE, verbose = FALSE, conf.level = 0.95)

## A total of 63,887 cattle need to be sampled (35,161 from population 1 and
## 28,726 from population 2) to meet the requirements of the study.
```

`epi.ssequb` *Sample size for a parallel equivalence or equality trial, binary outcome*

Description

Sample size for a parallel equivalence or equality trial, binary outcome.

Usage

```
epi.ssequb(treat, control, delta, n, power, r = 1, type = "equivalence",
   nfractional = FALSE, alpha = 0.05)
```

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 the absolute change in the outcome of interest that represents a clinically meaningful difference. For an equivalence trial the value entered for `delta` must be greater than zero.
`n`	scalar, the total number of study subjects in the trial.
`power`	scalar, the required study power.
`r`	scalar, the number in the treatment group divided by the number in the control group.
`type`	a character string indicating the type of analysis to be run. Options are `equality` and `equivalence`. If `type = equality` is selected argument `delta` is ignored.
`nfractional`	logical, return fractional sample size.
`alpha`	scalar, defining the desired alpha level.

Value

A list containing the following:

n.total	the total number of study subjects required.
n.treat	the required number of study subject in the treatment group.
n.control	the required number of study subject in the control group.
delta	the equivalence limit, as entered by the user.
power	the specified or calculated study power.

Note

Consider a clinical trial comparing two groups, a standard treatment (s) and a new treatment (n). A proportion of subjects in the standard treatment group experience the outcome of interest P_s and a proportion of subjects in the new treatment group experience the outcome of interest P_n.

For an equivalence trial the null hypothesis is:

$H_0 : P_n - P_s \leq -\delta$

$H_0 : P_n - P_s \geq +\delta$

and the alternative hypothesis is:

$H_1 : P_n - P_s > -\delta$

$H_1 : P_n - P_s < +\delta$

If the alternative hypothesis is accepted we conclude that P_n is therapeutically equivalent to P_s. For an equivalence trial a two-sided test is used.

For an equality trial the null hypothesis is:

$H_0 : P_n - P_s = 0$

and the alternative hypothesis is:

$H_1 : P_n - P_s \neq 0$

If the alternative hypothesis is accepted we conclude that P_n differs from P_s. For an equality trial a two-sided test is used.

Note that when:

$$sign(P_n - P_s - \delta) \neq sign(z_{1-\alpha} + z_{1-\beta})$$

there is no solution for study power. For typical values of α and β this would occur if $P_n - P_s - \delta < 0$. That is, when the targeted alternative is within the null hypothesis. The function issues a warning if these conditions are met.

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

A summary of the key features of superiority, equivalence and non-superiority trial comparisons is shown in the following table (adapted from Machin et al., 2018 [page 170] and Wang et al., 2017):

Test for	Null hypothesis	Alternative hypothesis	Test

Superiority	$H_0 : P_n - P_s \leq \delta$	$H_1 : P_n - P_s > \delta$	1-sided or 2-sided
Equivalence	$H_0 : P_n - P_s \leq -\delta$ $H_0 : P_n - P_s \geq +\delta$	$H_1 : P_n - P_s > -\delta$ $H_1 : P_n - P_s < +\delta$	Two 1-sided tests
Equality	$H_0 : P_n - P_s == 0$	$H_1 : P_n - P_s \neq 0$	2-sided
Non-inferiority	$H_0 : P_n - P_s \leq -\delta$	$H_1 : P_n - P_s > -\delta$	1-sided

References

Bennett J, Dismukes W, Duma R, Medoff G, Sande M, Gallis H, Leonard J, Fields B, Bradshaw M, Haywood H, McGee Z, Cate T, Cobbs C, Warner J, Alling D (1979). A comparison of amphotericin B alone and combined with flucytosine in the treatment of cryptoccal meningitis. New England Journal of Medicine 301, 126 - 131. DOI: 10.1056/nejm197907193010303.

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.

Machin D, Campbell MJ, Tan SB, Tan SH (2018). Sample Sizes for Clinical, Laboratory and Epidemiology Studies. Wiley Blackwell, New York.

Wang B, Wang H, Tu X, Feng C (2017). Comparisons of superiority, non-inferiority, and equivalence trials. Shanghai Archives of Psychiatry 29, 385 - 388. DOI: 10.11919/j.issn.1002-0829.217163.

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% and a
## power of 80% what would be a realistic sample size if the trial were
## to be repeated?

epi.ssequb(treat = 0.50, control = 0.50, delta = 0.20, n = NA, power = 0.80,
   r = 1, type = "equivalence", nfractional = FALSE, 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.ssequc *Sample size for a parallel equivalence or equality trial, continuous outcome*

Description

Sample size for a parallel equivalence or equality trial, continuous outcome.

Usage

```
epi.ssequc(treat, control, sigma, delta, n, power, r = 1, type = "equivalence",
   nfractional = FALSE, alpha = 0.05)
```

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.
sigma	the expected population standard deviation of the outcome of interest.
delta	the equivalence limit, expressed as the absolute change in the outcome of interest that represents a clinically meaningful difference. For an equivalence trial the value entered for delta must be greater than zero.
n	scalar, the total number of study subjects in the trial.
power	scalar, the required study power.
r	scalar, the number in the treatment group divided by the number in the control group.
type	a character string indicating the type of analysis to be run. Options are equality and equivalence. If type = equality is selected argument delta is ignored.
nfractional	logical, return fractional sample size.
alpha	scalar, defining the desired alpha level.

Value

A list containing the following:

n.total	the total number of study subjects required.
n.treat	the required number of study subject in the treatment group.
n.control	the required number of study subject in the control group.
delta	the equivalence limit, as entered by the user.
power	the specified or calculated study power.

Note

Consider a clinical trial comparing two groups, a standard treatment (s) and a new treatment (n). The mean of the outcome of interest for subjects receiving the standard treatment is N_s and the mean of the outcome of interest for the new treatment group is N_n.

For an equivalence trial the null hypothesis is:

$H_0 : N_n - N_s \leq -\delta$

$H_0 : N_n - N_s \geq +\delta$

and the alternative hypothesis is:

$H_1 : N_n - N_s > -\delta$

$H_1 : N_n - N_s < +\delta$

If the alternative hypothesis is accepted we conclude that N_n is therapeutically equivalent to N_s. For an equivalence trial a two-sided test is used.

For an equality trial the null hypothesis is:

$H_0 : N_n - N_s = 0$

and the alternative hypothesis is:

$H_1 : N_n - N_s \neq 0$

If the alternative hypothesis is accepted we conclude that N_n differs from N_s. For an equality trial a two-sided test is used.

Note that when:

$$sign(P_n - P_s - \delta) \neq sign(z_{1-\alpha} + z_{1-\beta})$$

there is no solution for study power. For typical values of α and β this would occur if $P_n - P_s - \delta < 0$. That is, when the targeted alternative is within the null hypothesis. The function issues a warning if these conditions are met.

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

Refer to the documentation for `epi.ssequb` for a comparison of the key features of superiority, equivalence and non-inferiority trials.

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.

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

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Machin D, Campbell MJ, Tan SB, Tan SH (2018). Sample Sizes for Clinical, Laboratory and Epidemiology Studies. Wiley Blackwell, New York.

Wang B, Wang H, Tu X, Feng C (2017). Comparisons of superiority, non-inferiority, and equivalence trials. Shanghai Archives of Psychiatry 29, 385 - 388. DOI: 10.11919/j.issn.1002-0829.217163.

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 needed to be enrolled in the trial? Assume 80% power and
## 95% significance.

epi.ssequc(treat = 94, control = 96, sigma = 8, delta = 5, n = NA,
   power = 0.80, r = 1, type = "equivalence", nfractional = FALSE,
   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.ssequc(treat = 20, control = 21, sigma = 10, delta = 5, n = NA,
   power = 0.80, r = 1, type = "equivalence", nfractional = FALSE,
   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.ssequc(treat = 20, control = 21, sigma = 10, delta = 5, n = 150,
   power = NA, r = 1, type = "equivalence", nfractional = FALSE,
   alpha = 0.05)

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


## EXAMPLE 3:
## A study is to be carried out to determine if the daily weight gain of calves
## (in kilograms) on two diets differ. The null hypothesis is that there is
## no difference in daily weight gain. The alternative hypothesis is that
## daily weight gains for the two groups differ. How many calves need to
## be enrolled into a study to detect a statistically significant difference
## in daily weight gain for the two groups? Assume daily weight gain for the
## treatment group is 0.70 kg per day and daily weight gain for the control
## group is 0.65 kg per day and the standard deviation of daily weight gain in
## calves of this age is 0.06. Assume power of 0.80 and alpha of 0.05.

epi.ssequc(treat = 0.70, control = 0.65, sigma = 0.06, delta = NA, n = NA,
   power = 0.80, r = 1, type = "equality", nfractional = FALSE,
   alpha = 0.05)

## A total of 48 calves need to be enrolled into the study: 24 in the treatment
## group and 24 in the control group.
```

`epi.ssninfb` *Sample size for a non-inferiority trial, binary outcome*

Description

Sample size for a non-inferiority trial, binary outcome.

Usage

```
epi.ssninfb(treat, control, delta, n, power, r = 1, nfractional = FALSE,
   alpha = 0.05)
```

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 the absolute change in the outcome of interest that represents a clinically meaningful difference. For a non-inferiority trial the value entered for `delta` must be greater than or equal to zero.
`n`	scalar, the total number of study subjects in the trial.
`power`	scalar, the required study power.

r	scalar, the number in the treatment group divided by the number in the control group.
nfractional	logical, return fractional sample size.
alpha	scalar, defining the desired alpha level.

Value

A list containing the following:

n.total	the total number of study subjects required.
n.treat	the required number of study subject in the treatment group.
n.control	the required number of study subject in the control group.
delta	the equivalence limit, as entered by the user.
power	the specified or calculated study power.

Note

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; and (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.

Consider a clinical trial comparing two groups, a standard treatment (s) and a new treatment (n). A proportion of subjects in the standard treatment group experience the outcome of interest P_s and a proportion of subjects in the new treatment group experience the outcome of interest P_n.

For a non-inferiority trial the null hypothesis is:

$H_0 : P_n - P_s \leq -\delta$

and the alternative hypothesis is:

$H_1 : P_n - P_s > -\delta$

If the alternative hypothesis is accepted we conclude that P_n is not inferior to P_s. For a non-inferiority trial a one-sided test is used.

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

Refer to the documentation for epi.ssequb for a comparison of the key features of superiority, equivalence and non-inferiority trials.

Author(s)

Many thanks to Aniko Szabo (Medical College of Wisconsin, Wisconsin USA) for improvements to the power calculations for this function and suggestions to improve the documentation.

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.

Machin D, Campbell MJ, Tan SB, Tan SH (2018). Sample Sizes for Clinical, Laboratory and Epidemiology Studies. Wiley Blackwell, New York.

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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. 90):
## A pharmaceutical company would like to conduct a clinical trial to
## compare the efficacy of two antimicrobial agents when administered orally
## to patients with skin infections. Assume the true mean cure rate of the
## treatment is 0.85 and the true mean cure rate of the control is 0.65.
## We consider the proportion cured in the treatment group minus the proportion
## cured in the control group (i.e., delta) of 0.10 or less to be of no clinical
## significance.

## Assuming a one-sided test size of 5% and a power of 80% how many
## subjects should be included in the trial?

epi.ssninfb(treat = 0.85, control = 0.65, delta = 0.10, n = NA, power = 0.80,
   r = 1, nfractional = FALSE, alpha = 0.05)

## A total of 50 subjects need to be enrolled in the trial, 25 in the
## treatment group and 25 in the control group.


## EXAMPLE 1 (cont.):
## Suppose only 40 subjects were enrolled in the trial, 20 in the treatment
## group and 20 in the control group. What is the estimated study power?

epi.ssninfb(treat = 0.85, control = 0.65, delta = 0.10, n = 40, power = NA,
   r = 1, nfractional = FALSE, alpha = 0.05)

## With only 40 subjects the estimated study power is 0.73.
```

```
## EXAMPLE 2:
## Assume the true mean cure rate for a treatment group to be 0.40 and the true
## mean cure rate for a control group to be the same, 0.40. We consider a
## difference of 0.10 in cured proportions (i.e., delta = 0.10) to be of no
## clinical importance.

## Assuming a one-sided test size of 5% and a power of 30% how many
## subjects should be included in the trial?

n <- epi.ssninfb(treat = 0.4, control = 0.4, delta = 0.10, n = NA, power = 0.3,
   r = 1, nfractional = TRUE, alpha = 0.05)$n.total
n

## A total of 120 subjects need to be enrolled in the trial, 60 in the
## treatment group and 60 in the control group.

## Re-run the function using n = 120 to confirm that power equals 0.30:

epi.ssninfb(treat = 0.4, control = 0.4, delta = 0.10, n = n, power = NA,
   r = 1, nfractional = TRUE, alpha = 0.05)$power

## With 120 subjects the estimated study power is 0.30.
```

`epi.ssninfc` *Sample size for a non-inferiority trial, continuous outcome*

Description

Sample size for a non-inferiority trial, continuous outcome.

Usage

```
epi.ssninfc(treat, control, sigma, delta, n, power, r = 1, nfractional = FALSE,
   alpha = 0.05)
```

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.
`sigma`	the expected population standard deviation of the outcome of interest.
`delta`	the equivalence limit, expressed as the absolute change in the outcome of interest that represents a clinically meaningful difference. For a non-inferiority trial the value entered for `delta` must be greater than or equal to zero.
`n`	scalar, the total number of study subjects in the trial.
`power`	scalar, the required study power.

r	scalar, the number in the treatment group divided by the number in the control group.
nfractional	logical, return fractional sample size.
alpha	scalar, defining the desired alpha level.

Value

A list containing the following:

n.total	the total number of study subjects required.
n.treat	the required number of study subject in the treatment group.
n.control	the required number of study subject in the control group.
delta	the equivalence limit, as entered by the user.
power	the specified or calculated study power.

Note

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; and (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.

Consider a clinical trial comparing two groups, a standard treatment (s) and a new treatment (n). In each group, the mean of the outcome of interest for subjects receiving the standard treatment is N_s and the mean of the outcome of interest for subjects receiving the new treatment is N_n. We specify the absolute value of the maximum acceptable difference between N_n and N_s as δ. For a non-inferiority trial the value entered for delta must be greater than or equal to zero.

For a non-inferiority trial the null hypothesis is:

$H_0 : N_n - N_s \leq -\delta$

and the alternative hypothesis is:

$H_1 : N_n - N_s > -\delta$

If the alternative hypothesis is accepted we conclude that N_n is not inferior to N_s. For a non-inferiority trial a one-sided test is used.

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

Refer to the documentation for epi.ssequb for a comparison of the key features of superiority, equivalence and non-inferiority trials.

Author(s)

Many thanks to Aniko Szabo (Medical College of Wisconsin, Wisconsin USA) for improvements to the power calculations for this function and suggestions to improve the documentation.

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.

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Wang B, Wang H, Tu X, Feng C (2017). Comparisons of superiority, non-inferiority, and equivalence trials. Shanghai Archives of Psychiatry 29, 385 - 388. DOI: 10.11919/j.issn.1002-0829.217163.

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. 61 - 62):
## 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 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 -0.05 unit change in LDL is a clinically
## meaningful difference. Assume the standard deviation of LDL is 0.10 units
## 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.ssninfc(treat = 0.20, control = 0.20, sigma = 0.10, delta = 0.05, n = NA,
   power = 0.80, r = 1, nfractional = FALSE, 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.sssimpleestb` *Sample size to estimate a binary outcome using simple random sampling*

Description

Sample size to estimate a binary outcome using simple random sampling.

Usage

```
epi.sssimpleestb(N = NA, Py, epsilon, error = "relative",
   se, sp, nfractional = FALSE, conf.level = 0.95)
```

Arguments

N	scalar integer, the total number of individuals eligible for inclusion in the study. If N = NA the number of individuals eligible for inclusion is assumed to be infinite.
Py	scalar number, an estimate of the population proportion to be estimated.
epsilon	scalar number, the maximum difference between the estimate and the unknown population value expressed in absolute or relative terms.
error	character string. Options are absolute for absolute error and relative for relative error.
se	the diagnostic sensitivity of the method used to detect positive outcomes (0 - 1).
sp	the diagnostic specificity of the method used to detect positive outcomes (0 - 1).
nfractional	logical, return fractional sample size.
conf.level	scalar number, the level of confidence in the computed result.

Details

If a value is entered for N.psu a finite population correction factor (Cochran 1977) is applied to the calculated sample size estimate. That is:

$$n_{adj} = \frac{n}{1 + \left(\frac{n}{N}\right)}$$

Value

Returns an integer defining the required sample size.

Note

The sample size calculation method implemented in this function follows the approach described by Humphry et al. (2004) accounting for imperfect diagnostic sensitivity and specificity.

If epsilon.r equals the relative error the sample estimate should not differ in absolute value from the true unknown population parameter d by more than epsilon.r * d.

References

Cochran WG (1977). Sampling Techniques. John Wiley and Sons, London.

Getachew T, Getachew G, Sintayehu G, Getenet M, Fasil A (2016). Bayesian estimation of sensitivity and specificity of Rose Bengal, complement fixation, and indirect ELISA tests for the diagnosis of bovine brucellosis in Ethiopia. Veterinary Medicine International. DOI: 10.1155/2016/8032753

Humphry RW, Cameron A, Gunn GJ (2004). A practical approach to calculate sample size for herd prevalence surveys. Preventive Veterinary Medicine 65: 173 - 188.

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:
## 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 seropositive to
## B. abortus. Calculate the required sample size assuming use of a test
## with perfect diagnostic sensitivity and specificity.

epi.sssimpleestb(N = NA, Py = 0.15, epsilon = 0.20,
   error = "relative", se = 1.00, sp = 1.00, nfractional = FALSE,
   conf.level = 0.95)

## A total of 545 cattle need to be sampled to meet the requirements of the
## survey.


## EXAMPLE 1 (continued):
## Why don't I get the same results as other sample size calculators? The
## most likely reason is misspecification of epsilon. Other sample size
## calculators (e.g., OpenEpi) require you to enter the absolute
## error (as opposed to relative error). For the example above the absolute
## error is 0.20 * 0.15 = 0.03. Re-run epi.simpleestb:

epi.sssimpleestb(N = NA, Py = 0.15, epsilon = 0.03,
   error = "absolute", se = 1.00, sp = 1.00, nfractional = FALSE,
   conf.level = 0.95)

## A total of 545 cattle need to be sampled to meet the requirements of the
## survey.


## EXAMPLE 1 (continued):
## The World Organisation for Animal Health (WOAH) recommends that the
```

```
## compliment fixation test (CFT) is used for bovine brucellosis prevalence
## estimation. Assume the diagnostic sensitivity and specficity of the bovine
## brucellosis CFT to be used is 0.94 and 0.88 respectively
## (Getachew et al. 2016). Re-calculate the required sample size
## accounting for imperfect diagnostic test performance.

n.crude <- epi.sssimpleestb(N = NA, Py = 0.15, epsilon = 0.20,
   error = "relative", se = 0.94, sp = 0.88, nfractional = FALSE,
   conf.level = 0.95)
n.crude

## A total of 1168 cattle need to be sampled to meet the requirements of the
## survey.


## EXAMPLE 1 (continued):
## Being seropositive to brucellosis is likely to cluster within herds.
## Otte and Gumm (1997) cite the intracluster 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 use of an imperfect diagnostic test and the presence
## of clustering of brucellosis positivity at the herd level we estimate that
## a total of 3166 cattle need to be sampled to meet the requirements of
## the survey.
```

`epi.sssimpleestc` *Sample size to estimate a continuous outcome using simple random sampling*

Description

Sample size to estimate a continuous outcome using simple random sampling.

Usage

```
epi.sssimpleestc(N = NA, xbar, sigma, epsilon, error = "relative",
   nfractional = FALSE, conf.level = 0.95)
```

Arguments

N	scalar integer, the total number of individuals eligible for inclusion in the study. If N = NA the number of individuals eligible for inclusion is assumed to be infinite.
xbar	scalar number, the expected mean of the continuous variable to be estimated.
sigma	scalar number, the expected standard deviation of the continuous variable to be estimated.
epsilon	scalar number, the maximum difference between the estimate and the unknown population value expressed in absolute or relative terms.
error	character string. Options are absolute for absolute error and relative for relative error.
nfractional	logical, return fractional sample size.
conf.level	scalar number, the level of confidence in the computed result.

Details

If a value is entered for N.psu a finite population correction factor (Cochran 1977) is applied to the calculated sample size estimate. That is:

$$n_{adj} = \frac{n}{1 + \left(\frac{n}{N}\right)}$$

Value

Returns an integer defining the required sample size.

Note

If epsilon.r equals the relative error the sample estimate should not differ in absolute value from the true unknown population parameter d by more than epsilon.r * d.

References

Cochran WG (1977). Sampling Techniques. John Wiley and Sons, London.

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; psigma <- (300 * 0.05)
epi.sssimpleestc(N = 20, xbar = pmean, sigma = psigma, epsilon = 0.20,
   error = "relative", nfractional = FALSE, conf.level = 0.95)

## Four clinics need to be sampled to meet the requirements of the survey.


## 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.sssimpleestc(N = 278, xbar = 200, sigma = 30, epsilon = 10,
   error = "absolute", nfractional = FALSE, conf.level = 0.95)

## A total of 28 deer need to be sampled to meet the requirements of the survey.
```

---

epi.ssstrataestb *Sample size to estimate a binary outcome using stratified random sampling*

Description

Sample size to estimate a binary outcome using stratified random sampling.

Usage

```
epi.ssstrataestb(strata.n, strata.Py, epsilon, error = "relative",
   nfractional = FALSE, conf.level = 0.95)
```

Arguments

strata.n	vector of integers, the number of individual listing units in each strata.
strata.Py	vector of numbers, the expected proportion of individual listing units with the outcome of interest for each strata.

epsilon	scalar number, the maximum difference between the estimate and the unknown population value expressed in absolute or relative terms.
error	character string. Options are absolute for absolute error and relative for relative error.
nfractional	logical, return fractional sample size.
conf.level	scalar number, 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.

Author(s)

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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:
## 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.ssstrataestb(strata.n, strata.Py, epsilon = 0.20, error = "relative",
   nfractional = FALSE, conf.level = 0.95)

## A total of 55 herds should be sampled: 11 small, 18 medium, and 28 large.
```

`epi.ssstrataestc` *Sample size to estimate a continuous outcome using a stratified random sampling design*

Description

Sample size to estimate a continuous outcome using a stratified random sampling design.

Usage

```
epi.ssstrataestc(strata.n, strata.xbar, strata.sigma, epsilon,
   error = "relative", nfractional = FALSE, conf.level = 0.95)
```

Arguments

`strata.n`	vector of integers, defining the number of individual listing units in each strata.
`strata.xbar`	vector of numbers, defining the expected means of the continuous variable to be estimated for each strata.
`strata.sigma`	vector of numbers, defining the expected standard deviation of the continous variable to be estimated for each strata.
`epsilon`	scalar number, the maximum difference between the estimate and the unknown population value expressed in absolute or relative terms.
`error`	character string. Options are `absolute` for absolute error and `relative` for relative error.
`nfractional`	logical, return fractional sample size.
`conf.level`	scalar number, 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.

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 (from 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.xbar <- c(0.164,0.166,0.236)
strata.sigma <- sqrt(c(0.245,0.296,0.436))
epi.ssstrataestc(strata.n, strata.xbar, strata.sigma, epsilon = 0.20,
   error = "relative", nfractional = FALSE, conf.level = 0.95)

## The number allocated to the under 45 years, 45 -- 64 years, and 65 years
## and over stratums should be 224, 187, and 150 (a total of 561). These
## results differ from the worked example provided in Levy and Lemeshow where
## certainty is set to approximately 99%.
```

---

epi.sssupb *Sample size for a parallel superiority trial, binary outcome*

Description

Sample size for a parallel superiority trial, binary outcome.

Usage

```
epi.sssupb(treat, control, delta, n, power, r = 1, sided.test,
   nfractional = FALSE, alpha = 0.05)
```

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 the absolute change in the outcome of interest that represents a clinically meaningful difference. For a superiority trial the value entered for delta must be greater than or equal to zero.
n	scalar, the total number of study subjects in the trial.
power	scalar, the required study power.
r	scalar, the number in the treatment group divided by the number in the control group.
sided.test	scalar, use a one- or two-sided test?
nfractional	logical, return fractional sample size.
alpha	scalar, defining the desired alpha level.

Value

A list containing the following:

n.total	the total number of study subjects required.
n.treat	the required number of study subject in the treatment group.
n.control	the required number of study subject in the control group.
delta	the equivalence limit, as entered by the user.
power	the specified or calculated study power.

Note

Consider a clinical trial comparing two groups, a standard treatment (s) and a new treatment (n). A proportion of subjects in the standard treatment group experience the outcome of interest P_s and a proportion of subjects in the new treatment group experience the outcome of interest P_n.

For a superiority trial the null hypothesis is:

$H_0 : P_n - P_s \leq \delta$

and the alternative hypothesis is:

$H_1 : P_n - P_s > \delta$

If the alternative hypothesis is accepted we conclude that P_n does not equal P_s. Regulatory agencies and most clinical trial guidelines recommend two-sided tests for superiority trials.

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

Refer to the documentation for epi.ssequb for a comparison of the key features of superiority, equivalence and non-inferiority trials.

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.

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

Machin D, Campbell MJ, Tan SB, Tan SH (2018). Sample Sizes for Clinical, Laboratory and Epidemiology Studies. Wiley Blackwell, New York.

Pocock SJ (1983). Clinical Trials: A Practical Approach. Wiley, New York.

Wang B, Wang H, Tu X, Feng C (2017). Comparisons of superiority, non-inferiority, and equivalence trials. Shanghai Archives of Psychiatry 29, 385 - 388. DOI: 10.11919/j.issn.1002-0829.217163.

Examples

```
## EXAMPLE 1 (from Chow S, Shao J, Wang H 2008, p. 91):
## 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.sssupb(treat = 0.85, control = 0.65, delta = 0.05, n = NA,
   power = 0.80, r = 1, sided.test = 1, nfractional = FALSE, 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.sssupc *Sample size for a parallel superiority trial, continuous outcome*

Description

Sample size for a parallel superiority trial, continuous outcome.

Usage

```
epi.sssupc(treat, control, sigma, delta, n, power, r = 1, sided.test,
   nfractional = FALSE, alpha = 0.05)
```

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.
sigma	the expected population standard deviation of the outcome of interest.

delta	the equivalence limit, expressed as the absolute change in the outcome of interest that represents a clinically meaningful difference. For a superiority trial the value entered for delta must be greater than or equal to zero.
n	scalar, the total number of study subjects in the trial.
power	scalar, the required study power.
r	scalar, the number in the treatment group divided by the number in the control group.
sided.test	scalar, use a one- or two-sided test?
nfractional	logical, return fractional sample size.
alpha	scalar, defining the desired alpha level.

Value

A list containing the following:

n.total	the total number of study subjects required.
n.treat	the required number of study subject in the treatment group.
n.control	the required number of study subject in the control group.
delta	the equivalence limit, as entered by the user.
power	the specified or calculated study power.

Note

Consider a clinical trial comparing two groups, a standard treatment (s) and a new treatment (n). The mean of the outcome of interest for subjects receiving the standard treatment is N_s and the mean of the outcome of interest for the new treatment group is N_n.

For a superiority trial the null hypothesis is:

$H_0 : N_n - N_s \leq \delta$

and the alternative hypothesis is:

$H_1 : N_n - N_s > \delta$

If the alternative hypothesis is accepted we conclude that N_n does not equal N_s. Regulatory agencies and most clinical trial guidelines recommend two-sided tests for superiority trials.

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

Refer to the documentation for epi.ssequb for a comparison of the key features of superiority, equivalence and non-inferiority trials.

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.

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

Machin D, Campbell MJ, Tan SB, Tan SH (2018). Sample Sizes for Clinical, Laboratory and Epidemiology Studies. Wiley Blackwell, New York.

Pocock SJ (1983). Clinical Trials: A Practical Approach. Wiley, New York.

Wang B, Wang H, Tu X, Feng C (2017). Comparisons of superiority, non-inferiority, and equivalence trials. Shanghai Archives of Psychiatry 29, 385 - 388. DOI: 10.11919/j.issn.1002-0829.217163.

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.sssupc(treat = 20, control = 20, sigma = 10, delta = 5, n = NA,
   power = 0.80, r = 1, sided.test = 1, nfractional = FALSE, 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.ssxsectn` *Sample size, power or minimum detectable prevalence ratio or odds ratio for a cross-sectional study*

Description

Sample size, power or minimum detectable prevalence ratio or odds ratio for a cross-sectional study.

Usage

```
epi.ssxsectn(N = NA, pdexp1, pdexp0, pexp = NA, n, power, r = 1,
   design = 1, sided.test = 2, nfractional = FALSE, conf.level = 0.95)
```

Arguments

N	scalar integer, the total number of individuals eligible for inclusion in the study. If N = NA the number of individuals eligible for inclusion is assumed to be infinite.
pdexp1	the expected prevalence of the outcome in the exposed group (0 to 1).
pdexp0	the expected prevalence of the outcome in the non-exposed group (0 to 1).
pexp	the expected prevalence of exposure to the hypothesised risk factor in the population (0 to 1).
n	scalar, defining the total number of subjects in the study (i.e., the number in both the exposed and unexposed groups).
power	scalar, the required study power.
r	scalar, the number in the exposed group divided by the number in the unexposed 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 outcome incidence risk in the exposed group is greater than or less than the outcome incidence risk in the unexposed group. Use a one-sided test to evaluate whether or not the outcome incidence risk in the exposed group is greater than the outcome incidence risk in the unexposed group.
nfractional	logical, return fractional sample size.
conf.level	scalar, defining the level of confidence in the computed result.

Details

The methodology in this function follows the methodology described in Chapter 8 of Woodward (2014), pp. 295 - 329.

If a value is entered for N.psu a finite population correction factor (Cochran 1977) is applied to the calculated sample size estimate. That is:

$$n_{adj} = \frac{n}{1 + \left(\frac{n}{N}\right)}$$

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 exposed (treatment) group compared with the non-exposed (control) group.
n.exp1	the total number of subjects in the exposed (treatment) group for the specified level of confidence and power, respecting the requirement for r times as many individuals in the exposed (treatment) group compared with the non-exposed (control) group.

n.exp0	the total number of subjects in the non-exposed (control) group for the specified level of confidence and power, respecting the requirement for r times as many individuals in the exposed (treatment) group compared with the non-exposed (control) group.
power	the power of the study given the number of study subjects, the expected effect size and level of confidence.
pr	the prevalence of the outcome in the exposed group divided by the prevalence of the outcome in the unexposed group (the prevalence ratio).
or	the odds of the outcome in the exposed group divided by the odds of the outcome in the unexposed group (the odds 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 pdexp0, pexp, n, and power to return a value for the prevalence ratio pr and odds ratio or. In this situation, the lower value of pr represents the maximum detectable prevalence ratio that is less than 1; the upper value of pr represents the minimum detectable prevalence ratio greater than 1. A value for pexp doesn't need to be entered if you want to calculate sample size or study power.

When calculating study power or minimum detectable prevalence risk ratio when finite.correction = TRUE the function takes the values of n and N entered by the user and back-calculates a value of n assuming an infinite population. Values for power, pr and or are then returned, assuming the back-calculated value of n is equivalent to the value of n entered by the user.

See the documentation for epi.sscohortc for an example using the design facility implemented in this function.

References

Cochran WG (1977). Sampling Techniques. John Wiley and Sons, London.

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

Mittleman MA (1995). Estimation of exposure prevalence in a population at risk using data from cases and an external estimate of the relative risk. Epidemiology 6: 551 - 553.

Woodward M (2014). Epidemiology Study Design and Data Analysis. Chapman & Hall/CRC, New York, pp. 295 - 329.

Examples

```
## EXAMPLE 1:
## A cross-sectional study is to be carried out to quantify the association
## between farm management type (intensive, extensive) and evidence of
## Q fever in dairy goat herds. The investigators would like to be 0.80 sure
## of being able to detect when the risk ratio of Q fever is 2.0 for
## intensively managed herds, using a 0.05 significance test. Previous evidence
## suggests that the prevalence of Q fever in extensively managed dairy goat
## herds is 5 per 100 herds at risk and the prevalence of intensively managed
```

```
## herds in the population (the prevalence of exposure) is around 0.20.

## Assuming equal numbers of intensively managed and extensively managed
## herds will be sampled, how many herds need to be enrolled into the study?
## You estimate that there are around 60 dairy goat herds in your study area.

pdexp1 = 2.0 * (5 / 100); pdexp0 = 5 / 100
epi.ssxsectn(N = 60, pdexp1 = pdexp1, pdexp0 = pdexp0, pexp = 0.20, n = NA,
   power = 0.80, r = 1, design = 1, sided.test = 2,
   nfractional = FALSE, conf.level = 0.95)

## A total of 58 of the 60 herds need to be enrolled into the study
## (29 intensively managed and 29 extensively managed herds).


## EXAMPLE 2:
## Say, for example, we're only able to enrol 45 herds into the study
## described above. What is the minimum and maximum detectable prevalence
## ratio and minimum and maximum detectable odds ratio?

epi.ssxsectn(N = 60, pdexp1 = NA, pdexp0 = pdexp0, pexp = 0.20, n = 45,
   power = 0.80, r = 1, design = 1, sided.test = 2,
   nfractional = FALSE, conf.level = 0.95)

## The minimum detectable prevalence ratio >1 is 3.64. The maximum detectable
## prevalence ratio <1 is 0.

## The minimum detectable odds ratio >1 is 4.65. The maximum detectable
## odds ratio <1 is 0.
```

`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, method = "exact", digits = 2, conf.level = 0.95)

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

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

Arguments

dat	a vector of length four, an object of class table or an object of class grouped_df from package dplyr containing the individual cell frequencies (see below).
method	a character string indicating the method to use. Options are method = "exact", method = "wilson", method = "agresti", method = "clopper-pearson" and method = "jeffreys".
digits	scalar, number of digits to be reported for print output. Must be an integer of either 2, 3 or 4.
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

The required 2 by 2 table format for epi.tests is shown below. Columns list outcome (e.g., true disease) status: counts of outcome positive study units in column 1 and outcome negative study units in column 2. Rows list test status: counts of test positive study units in row 1 and counts of test negative study units in row 2. The labels a, b, c and d in the table below correspond to the order of study unit counts when argument dat is a vector.

	Outcome +	Outcome -	Total
Test +	a	b	a+b
Test -	c	d	c+d
Total	a+c	b+d	a+b+c+d

When method = "exact" exact binomial confidence limits are calculated for test sensitivity, specificity, and positive and negative predictive value (see Collett 1999 for details).

When method = "wilson" Wilson's confidence limits are calculated for test sensitivity, specificity, and positive and negative predictive value (see Rothman 2012 for details).

When method = "agresti" Agresti's confidence limits are calculated for test sensitivity, specificity, and positive and negative predictive value (see Agresti and Coull 1998 for details).

When method = "clopper-pearson" Clopper-Pearson's confidence limits are calculated for test sensitivity, specificity, and positive and negative predictive value (see Clopper and Pearson 1934 for details).

When method = "jeffreys" Jeffrey's confidence limits are calculated for test sensitivity, specificity, and positive and negative predictive value (see Brown et al., 2001 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 patients 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

A data frame of class `epi.tests` listing:

`statistic`	The name of the outcome measure.
`est`	The point estimate of the listed outcome measure.
`lower`	The lower bound of the confidence interval of the listed outcome measure.
`upper`	The upper bound of the confidence interval of the listed outcome measure.

The following outcome measures are returned:

`tp`	True prevalence.
`ap`	Apparent prevalence.
`se`	Diagnostic test sensitivity.
`sp`	Diagnostic test specificity.
`diag.ac`	Diagnostic accuracy (the correctly classified proportion).
`diag.or`	Diagnostic odds ratio.
`nndx`	The number needed to diagnose.
`youden`	Youden's index.
`pv.pos`	Positive predictive value.
`pv.neg`	Negative predictive value.
`lr.pos`	Likelihood ratio of a positive test.
`lr.neg`	Likelihood ratio of a negative test.
`p.rout`	The proportion of subjects with the outcome ruled out.
`p.rin`	The proportion of subjects with the outcome ruled in.
`p.tpdn`	The proportion of true outcome negative subjects that test positive (false T+ proportion for D-).
`p.tndp`	The proportion of true outcome positive subjects that test negative (false T- proportion for D+).
`p.dntp`	The proportion of test positive subjects that are outcome negative (false T+ proportion for T+).
`p.dptn`	The proportion of test negative subjects that are outcome positive (false T- proportion for T-).

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)

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References

Agresti A, Coull B (1998). Approximate is better than 'exact' for interval estimation of binomial proportions. The American Statistician 52. DOI: 10.2307/2685469.

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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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Wilson EB (1927) Probable inference, the law of succession, and statistical inference. Journal of the American Statistical Association 22: 209 - 212.

Examples

```
## EXAMPLE 1 (from Scott et al. 2008, Table 1):
## A new diagnostic test was trialled on 1586 patients. Of 744 patients that
## were disease positive, 670 were test positive. Of 842 patients that were
## disease negative, 640 were test negative. What is the likeliood ratio of
## a positive test? What is the number needed to diagnose?

dat.v01 <- c(670,202,74,640)
rval.tes01 <- epi.tests(dat.v01, method = "exact", digits = 2,
   conf.level = 0.95)
print(rval.tes01)

## Test sensitivity is 0.90 (95% CI 0.88 to 0.92). Test specificity is
## 0.76 (95% CI 0.73 to 0.79). The likelihood ratio of a positive test
## is 3.75 (95% CI 3.32 to 4.24).

## What is the number needed to diagnose?
rval.tes01$detail

## 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.


## EXAMPLE 2:
## Same as Example 1 but showing how a 2 by 2 contingency table can be prepared
## using tidyverse:

## Not run:
library(tidyverse)

## Generate a data set listing test results and true disease status:
dis <- c(rep(1, times = 744), rep(0, times = 842))
tes <- c(rep(1, times = 670), rep(0, times = 74),
   rep(1, times = 202), rep(0, times = 640))
dat.df02 <- data.frame(dis, tes)

tmp.df02 <- dat.df02 %>%
  mutate(dis = factor(dis, levels = c(1,0), labels = c("Dis+","Dis-"))) %>%
  mutate(tes = factor(tes, levels = c(1,0), labels = c("Test+","Test-"))) %>%
  group_by(tes, dis) %>%
  summarise(n = n())
tmp.df02

## View the data in conventional 2 by 2 table format:
pivot_wider(tmp.df02, id_cols = c(tes), names_from = dis, values_from = n)

rval.tes02 <- epi.tests(tmp.df02, method = "exact", digits = 2,
   conf.level = 0.95)
summary(rval.tes02)

## End(Not run)
```

```
## Test sensitivity is 0.90 (95% CI 0.88 to 0.92). Test specificity is
## 0.76 (95% CI 0.73 to 0.79). The likelihood ratio of a positive test
## is 3.75 (95% CI 3.32 to 4.24).


## EXAMPLE 3:
## A biomarker assay has been developed to identify patients that are at
## high risk of experiencing myocardial infarction. The assay varies on
## a continuous scale, from 0 to 1. Researchers believe that a biomarker
## assay result of greater than or equal to 0.60 renders a patient test
## positive, that is, at elevated risk of experiencing a heart attack
## over the next 12 months.

## Generate data consistent with the information provided above. Assume the
## prevalence of high risk subjects in your population is 0.35:
set.seed(1234)
dat.df03 <- data.frame(out = rbinom(n = 200, size = 1, prob = 0.35),
   bm = runif(n = 200, min = 0, max = 1))

## Classify study subjects as either test positive or test negative
## according to their biomarker test result:
dat.df03$test <- ifelse(dat.df03$bm >= 0.6, 1, 0)

## Generate a two-by-two table:
dat.tab03 <- table(dat.df03$test, dat.df03$out)[2:1,2:1]
rval.tes03 <- epi.tests(dat.tab03, method = "exact", digits = 2,
   conf.level = 0.95)
print(rval.tes03)

## What proportion of subjects are ruled out as being at high risk of
## myocardial infarction?
rval.tes03$detail[rval.tes03$detail$statistic == "p.rout",]
## Answer: 0.61 (95% CI 0.54 to 0.68).

## What proportion of subjects are ruled in as being at high risk of
## myocardial infarction?
rval.tes03$detail[rval.tes03$detail$statistic == "p.rin",]
# Answer: 0.38 (95% CI 0.32 to 0.45).

## What is the proportion of false positive results? That is, what is the
## proportion of test positive individuals among those that are disease
## negative, p.tpdn?
rval.tes03$detail[rval.tes03$detail$statistic == "p.tpdn",]
# Answer: 0.37 (95% CI 0.29 to 0.45).

## What is the proportion of false negative results? That is, what is the
## proportion of test negative individuals among those that are disease
## positive, p.tndp?
rval.tes03$detail[rval.tes03$detail$statistic == "p.tndp",]
# Answer: 0.58 (95% CI 0.44 to 0.70).
```

rsu.adjrisk *Adjusted risk values*

Description

Calculates adjusted risk estimates for given relative risk and population proportions. This is an intermediate calculation in the calculation of effective probability of infection for risk-based surveillance activities.

Usage

```
rsu.adjrisk(rr, ppr)
```

Arguments

rr	vector or matrix, defining the relative risk values for each strata in the population. See details.
ppr	vector of length rr defining the population proportions in each strata.

Details

On some occasions there is interest in calculating adjusted risk values for a series of relative risk estimates drawn from (for example) a probability distribution. In this situation a matrix is passed to argument rr with the columns of the matrix corresponding to the number of risk strata and the rows corresponding to the number of iterations for simulation. When data are entered in this format rsu.adjrisk returns a matrix of adjusted risk values of the same dimension. See Example 3, below.

Value

A vector of adjusted risk values listed in order of rr.)

References

Martin P, Cameron A, Greiner M (2007). Demonstrating freedom from disease using multiple complex data sources 1: A new methodology based on scenario trees. Preventive Veterinary Medicine 79: 71 - 97.

Examples

```
## EXAMPLE 1:
## The relative risk of a given disease in an area of your country is 5
## compared with a known reference 'low risk' area. A recent census shows that
## 10% of the population are resident in the high risk area and 90%
## are resident in the low risk area.   .

## Calculate the adjusted relative risks for each area.

rsu.adjrisk(rr = c(5,1), ppr = c(0.10,0.90))
```

```
## The adjusted relative risks for the high and low risk areas are 3.6 and
## 0.7, respectively.


## EXAMPLE 2:
## Re-calculate the adjusted relative risks assuming there are 'high',
## 'medium' and 'low' risk areas. The relative risks for the high, medium
## and low risk areas are 5, 3 and 1, respectively. Population proportions for
## each area are 0.10, 0.10 and 0.80, respectively.

rsu.adjrisk(rr = c(5,3,1), ppr = c(0.10,0.10,0.80))

## The adjusted relative risks for the high, medium and low risk areas are
## 3.1, 1.9 and 0.6, respectively.


## EXAMPLE 3:
## Consider now the situation where we are not certain of our relative risk
## estimates for the high, medium and low risk areas described in Example 2
## so we ask a group of experts for their opinion. Minimum, mode and maximum
## relative risk estimates for the high and medium risk areas are defined
## using a PERT distribution. For the high risk area the mode of the
## relative risk is 5 with a minimum of 3 and a maximum of 20. For the medium
## risk area the mode of the relative risk is 3 with a minimum of 2 and a
## maximum of 20. As before, the population proportions for each area are
## 0.10, 0.10 and 0.80, respectively. Take 10 random draws from a PERT
## distribution (using the rpert function in package mc2d) and calculate
## the adjusted relative risks for each draw:

## Not run:
## Set up an empty matrix to collect the simulated relative risk values:
nsims <- 10; nrcat <- 3
rr <- matrix(NA, nrow = nsims, ncol = nrcat)

## Use the mc2d package to take nsims random draws from the PERT distribution:
rr[,1] <- mc2d::rpert(n = nsims, min = 3, mode = 5, max = 20)
rr[,2] <- mc2d::rpert(n = nsims, min = 2, mode = 3, max = 5)

## The low risk area is the reference, so its relative risk values are 1:
rr[,3] <- 1

## Population proportions:
ppr <- c(0.10,0.10,0.80)

rval.df <- rsu.adjrisk(rr, ppr)
summary(rval.df)

## The median adjusted relative risks for the high, medium and low risk area
## are 3.6, 1.6 and 0.5 (respectively). The minimum adjusted relative risks
## are 2.5, 1.3 and 0.39, repectively. The maximum adjusted relative risks
## are 5.5, 2.3 and 0.72, respectively.
```

```
## End(Not run)
```

`rsu.dxtest` *Sensitivity and specificity of diagnostic tests interpreted in series or parallel*

Description

Calculates the sensitivity and specificity of two or three diagnostic tests interpreted in series or parallel.

Usage

```
rsu.dxtest(se, sp, covar.pos, covar.neg, tconf.int, method = "exact",
   interpretation = "series", conf.int = 0.95, nsim = 999)
```

Arguments

`se`	a matrix of diagnostic test sensitivities. For tests without confidence intervals for sensitivity this will be a 2 or 3-row, 1-column matrix with rows 1 to 3 representing diagnostic tests and column 1 listing the point estimate of diagnostic sensitivity. For tests with confidence intervals for sensitivity this will be a 2 or 3-row, 3-column matrix with rows 1 to 3 representing diagnostic tests and columns 1, 2 and listing the point estimate, the lower bound of the sensitivity confidence interval and the upper bound of the sensitivity confidence interval, respectively.
`sp`	a matrix of diagnostic test specificities. For tests without confidence intervals for specificity this will be a 2 or 3-row, 1-column matrix with rows 1 to 3 representing diagnostic tests and column 1 listing the point estimate of diagnostic specificity. For tests with confidence intervals for specificity this will be a 2 or 3-row, 3-column matrix with rows 1 to 3 representing diagnostic tests and columns 1, 2 and listing the point estimate, the lower bound of the specificity confidence interval and the upper bound of the specificity confidence interval, respectively.
`covar.pos`	a vector of length either two or four defining the covariance between test results for the disease positive group. For two diagnostic tests `covar.pos` is a vector of length one. For three diagnostic tests `covar.pos` is a vector of length four listing (in order) the covariance between test 1 and 2, test 1 and 3, test 2 and 3 and tests 1, 2 and 3. See the examples, below for details.
`covar.neg`	a vector of length either two or four defining the covariance between test results for the disease negative group. For two diagnostic tests `covar.neg` is a vector of length one. For three diagnostic tests `covar.neg` is a vector of length four listing (in order) the covariance between test 1 and 2, test 1 and 3, test 2 and 3 and tests 1, 2 and 3. See the examples, below for details.

tconf.int	scalar, the magnitude of the confidence interval for the listed diagnostic test performance measures (se and sp).
method	a character string indicating the method used to calculate the confidence intervals for se and sp. Options are method = "exact", method = "wilson", method = "agresti", method = "clopper-pearson" and method = "jeffreys".
interpretation	a character string indicating how the test results should be interpreted. Options are series or parallel.
conf.int	magnitude of the returned confidence interval for sensitivity and specificity if tests are interpreted in series or parallel. Must be a single number between 0 and 1.
nsim	scalar, defining the number of simulations to be used to estimate confidence interval for sensitivity and specificity if tests are interpreted in series or parallel.

Value

A list comprised of four elements:

independent	a data frame listing sensitivity se and specificity sp assuming the tests are independent.
dependent	a data frame listing sensitivity se and specificity sp calculated using the values of covar.pos and covar.neg, as entered by the user.
covar.pos	a data frame listing the covariance between test results for the disease positive group, as entered by the user.
covar.neg	a data frame listing the covariance between test results for the disease negative group, as entered by the user.

If covar.pos = 0 and covar.neg = 0 (for the two test situation) data frames independent and dependent will be identical.

Note

For interpretation = "series" a subject is declared test positive if both of the tests performed return a positive result. For interpretation = "parallel" a subject is declared test positive if one of the tests performed return a positive result. Intepreting test results in series increases diagnostic specificity. Interpreting test results in parallel increases diagnostic sensitivity.

For the two test situation covar.pos is a vector of length one quantifying the covariance between between the two tests for the disease positive group. For the three test situation covar.pos is a vector of length four listing (in order) the the covariance between test 1 and 2, test 1 and 3, test 2 and 3 and tests 1, 2 and 3 for the disease positive group:

Element	Test pair
1	Test 1 - Test 2
2	Test 1 - Test 3
3	Test 2 - Test 3
4	Test 1, 2, and 3

For the two test situation `covar.neg` is a vector of length one quantifying the covariance between between the two tests for the disease negative group. For the three test situation `covar.neg` is a vector of length four listing (in order) the the covariance between test 1 and 2, test 1 and 3, test 2 and 3 and tests 1, 2 and 3 for the disease negative group:

Element	Test pair
1	Test 1 - Test 2
2	Test 1 - Test 3
3	Test 2 - Test 3
4	Test 1, 2, and 3

How do I work out appropriate values for `covar.pos` and `covar.neg`? Assume you have two diagnostic tests — an indirect fluorescent antibody test (IFAT) and a polymerase chain reaction (PCR). The diagnostic sensitivity and specificity of the IFAT is 0.784 and 0.951, respectively. The diagnostic sensitivity and specificity of the PCR is 0.926 and 0.979, respectively. These tests are used on a group of individuals known to be disease positive and a group of individuals known to be disease negative. Results for the disease positive group are as follows:

	IFAT		
PCR	Pos	Neg	Total
Pos	134	29	163
Neg	4	9	13
Total	138	38	176

Results for the disease negative group are as follows:

	IFAT		
PCR	Pos	Neg	Total
Pos	0	12	12
Neg	28	534	562
Total	28	546	574

The observed proportion of disease positive individuals with a positive test result to both tests as `p111`. For this example `p111 = 134 / 176 = 0.761`.

The observed proportion of disease negative individuals with a negative test result to both tests as p000. For this example p000 = 534 / 574 = 0.930.

Covariance for the disease positive group: covar.pos = p111 - se[1] * se[2] = 0.761 - 0.784 * 0.926 = 0.035.

Covariance for the disease negative group: covar.neg = p000 - sp[1] * sp[2] = 0.930 - 0.951 * 0.979 = -0.001.

The covariance for the disease positive group is small. The covariance for the disease negative group is negligible.

References

Dohoo I, Martin S, Stryhn H (2009). Veterinary Epidemiologic Research. AVC Inc Charlottetown, Prince Edward Island, Canada.

Gardner I, Stryhn H, Lind P, Collins M (2000). Conditional dependence between tests affects the diagnosis and surveillance of animal diseases. Preventive Veterinary Medicine 45: 107 - 122.

Jones G, Johnson W, Hanson T, Christensen R (2010). Identifiability of models for multiple diagnostic testing in the absence of a gold standard. Biometrics 66: 855 - 863. DOI: 10.1111/j.1541-0420.2009.01330.x.

Martin S, Meek A, Willeberg P (1987). Veterinary Epidemiology Principles and Methods. Iowa State University Press Ames.

McClure C, Hammell K, Stryhn H, Dohoo I, Hawkins L (2005). Application of surveillance data in evaluation of diagnostic tests for infectious salmon anemia. Diseases of Aquatic Organisms 63: 119 - 127. DOI: 10.3354/dao063119.

Toft N, Akerstedt J, Tharaldsen J, Hopp P (2007). Evaluation of three serological tests for diagnosis of Maedi-Visna virus infection using latent class analysis. Veterinary Microbiology 120: 77 - 86.

Examples

```
## EXAMPLE 1:
## You would like to confirm the absence of disease in a study area. You
## 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. You need to make sure that an individual
## that returns a positive test really has disease, so the tests will be
## interpreted in series (to improve specificity).

## What is the diagnostic sensitivity and specificity of this testing
## regime?

se <- matrix(c(0.90,0.95), ncol = 1, byrow = TRUE); se
sp <- matrix(c(0.80,0.85), ncol = 1, byrow = TRUE); sp

rsu.dxtest(se = se, sp = sp, covar.pos = 0 , covar.neg = 0,
   tconf.int = 0.95, method = "exact", interpretation = "series",
   conf.int = 0.95, nsim = 999)

## Interpretation of these tests in series returns a diagnostic sensitivity
## of 0.855 and a diagnostic specificity of 0.970.
```

```
## EXAMPLE 2 (from Dohoo, Martin and Stryhn p 113):
## An IFAT and PCR are to be used to diagnose infectious salmon anaemia (IFA).
## Counts of IFA positive salmon that tested positive to the IFAT and PCR and
## counts of IFA negative salmon that tested positive to the IFAT and PCR are
## shown above. Calculate the sensitivity and specificity of the two tests
## and a 95% confidence interval for sensitivity and specificity of the
## two tests using the exact method.

test <- rep(c("ifat","pcr"), each = 2)
perf <- rep(c("se","sp"), times = 2)
num <- c(138,546,163,562)
den <- c(176,574,176,574)
dat.df <- data.frame(test, perf, num, den)

tmp <- epi.conf(dat = as.matrix(dat.df[,3:4]), ctype = "prevalence",
   method = "exact", N = 1000, design = 1, conf.level = 0.95)
dat.df <- cbind(dat.df, tmp); dat.df

## The diagnostic sensitivity and specificity of the IFAT is 0.784
## (95% CI 0.716 to 0.842) and 0.951 (95% CI 0.930 to 0.967), respectively.

## The diagnostic sensitivity and specificity of the PCR is
## 0.926 (95% CI 0.877 to 0.960) and 0.979 (95% CI 0.964 to 0.989),
## respectively. It is known that the two tests are dependent,
## with positive and negative covariances calculated above. What is the
## expected sensitivity and specificity if the tests are to interpreted
## in parallel?

se <- matrix(c(0.784,0.716,0.842,0.926,0.877,0.960), ncol = 3,
   byrow = TRUE); se
sp <- matrix(c(0.951,0.930,0.967,0.979,0.964,0.989), ncol = 3,
   byrow = TRUE); sp

rsu.dxtest(se = se, sp = sp, covar.pos = 0.035, covar.neg = -0.001,
   tconf.int = 0.95, method = "exact", interpretation = "parallel",
   conf.int = 0.95, nsim = 999)

## Interpreting test results in parallel and accounting for the lack of
## test indepdendence returns a diagnostic sensitivity of 0.949 (95% CI 0.938
## to 0.957) and diagnostic specificity of 0.929 (95% CI 0.906 to 0.947).


## EXAMPLE 3:
## Three diagnostic tests for Brucella suis in dogs are available: the Rose
## Bengal test (RBT), complement fixation (CFT) and an c-ELISA. The diagnostic
## sensitivities of the three tests are 0.869, 0.873 and 0.897, respectively.
## The diagnostic specificities of the three tests are 0.895, 0.905, and 0.915,
## respectively.

## For disease positive groups the covariance between test results are
## as follows:
```

```
## RBT - CFT: 0.071
## RBT - c-ELISA: 0.018
## CFT - c-ELISA: 0.015
## RBT - CFT - c-ELISA: -0.001

covp012 <- 0.071
covp013 <- 0.018
covp023 <- 0.015
covp123 <- -0.001
covp <- c(covp012,covp013,covp023,covp123)

## For disease negative groups the covariance between test results are
## as follows:

## RBT - CFT: 0.076
## RBT - c-ELISA: 0.062
## CFT - c-ELISA: 0.062
## RBT - CFT - c-ELISA: 0.049

covn012 <- 0.076
covn013 <- 0.062
covn023 <- 0.062
covn123 <- 0.049
covn <- c(covn012,covn013,covn023,covn123)

## What is the expected diagnostic sensitivity and specificity if all three
## tests are run on an individual and interpreted in parallel?

se <- matrix(c(0.869,0.873,0.897), ncol = 1, byrow = TRUE); se
sp <- matrix(c(0.895,0.905,0.915), ncol = 1, byrow = TRUE); sp

rsu.dxtest(se = se, sp = sp, covar.pos = covp, covar.neg = covn,
   tconf.int = 0.95, method = "exact", interpretation = "parallel",
   conf.int = 0.95, nsim = 999)

## Interpreting the test results in parallel and accounting for depdendence
## between the three tests returns a diagnostic sensitivity of
## 0.991 and a diagnostic specificity of 0.873. If we didn't account for test
## dependence our estimate of diagnostic sensitivity and specificity would be
## 0.998 and 0.741, respectively.

## What is the expected sensitivity and specificity if all three
## tests are run on an individual and interpreted in series?

rsu.dxtest(se = se, sp = sp, covar.pos = covp, covar.neg = covn,
   tconf.int = 0.95, method = "exact", interpretation = "series",
   conf.int = 0.95, nsim = 999)

## Interpreting the test results in series and accounting for depdendence
## between the three tests returns a diagnostic sensitivity of
## 0.774 and a diagnostic specificity of 1.000.
```

`rsu.epinf` *Effective probability of disease*

Description

Calculates the effective probability of disease (adjusted design prevalence) for each risk group within a population.

Usage

```
rsu.epinf(pstar, rr, ppr)
```

Arguments

`pstar`	scalar, the design prevalence.
`rr`	vector, defining the relative risk values for each strata in the population.
`ppr`	vector of length `rr` defining the population proportions in each strata.

Value

A list of comprised of two elements:

`epinf`	a vector listing the effective probability of infection listed in order of `rr`.
`adj.risk`	a vector listing the adjusted risk values listed in order of `rr`.

Examples

```
## EXAMPLE 1:
## For a given disease of interest you believe that there is a 'high risk'
## and 'low risk' area in your country. The risk of disease in the high risk
## area compared with the low risk area is 5. A recent census shows that
## 10% of the population are resident in the high risk area and 90%
## are resident in the low risk area. You elect to set a design prevalence
## of 0.10.

## Calculate the effective probability of infection for each area.

rsu.epinf(pstar = 0.1, rr = c(5,1), ppr = c(0.10,0.90))

## The effective probabilities of infection for the high and low risk areas
## are 0.36 and 0.07, respectively.


## EXAMPLE 2:
## Re-calculate the effective probabilities of infection assuming there are
## 'high', 'medium' and 'low' risk areas. The risk of disease in the
## medium risk area compared with the low risk area is 3. Population
## proportions for each area are 0.10, 0.10 and 0.80, respectively.
```

```
rsu.epinf(pstar = 0.10, rr = c(5,3,1), ppr = c(0.10,0.10,0.80))

## The effective probabilities of infection for the high, medium and low
## risk areas are 0.31, 0.19 and 0.06, respectively.
```

`rsu.pfree.equ` *Equilibrium probability of disease freedom assuming representative or risk based sampling*

Description

Calculates the long-term equilibrium probability of disease freedom and equilibrium prior probability of freedom, after discounting for the probability that disease has been introduced into the population and assuming population sensitivity and probability of introduction are constant over time. It does not specify how long it might take to reach equilibrium.

Usage

```
rsu.pfree.equ(se.p, p.intro)
```

Arguments

`se.p`	scalar or vector, the surveillance system (population-level) sensitivity for the given time period.
`p.intro`	scalar or vector of the same length as `sep` representing the probability of disease introduction for time period.

Value

A list comprised of two elements:

`epfree`	a vector listing the equilibrium probability of disease freedom.
`depfree`	a vector listing the discounted equilibrium probability of disease freedom.

Examples

```
## EXAMPLE 1:
## The current (ongoing) surveillance system for a given disease in your
## country has been estimated to have a population sensitivity of 0.60 per
## time period (one year). Assuming the probability of disease introduction
## per unit time is 0.02, what is the eventual plateau level for confidence
## of freedom and how long will it take to reach this level, assuming a
# prior (starting) confidence of freedom of 0.50?

## Firstly, estimate the equilibrium (plateau) confidence of freedom:
```

```
conf.eq <- rsu.pfree.equ(se.p = 0.60, p.intro = 0.02)
conf.eq

## The equilibrium discounted probability of disease freedom is 0.986.

## Next, calculate confidence of freedom over 20 time periods for se.p = 0.60
## and p.intro = 0.02:

rval.df <- rsu.pfree.rs (se.p = rep(0.6, times = 20),
   p.intro = rep(0.02, times = 20), prior = 0.50)
head(rval.df)

## When does the confidence of freedom first reach the equilibrium value
## (rounded to 3 digits)?

rsep.p <- which(rval.df$pfree >= round(conf.eq$depfree, digits = 3))
rsep.p[1]

## It takes 9 time periods (years) to reach the equilibrium level of 0.986.


## EXAMPLE 2:
## You have been asked to design a surveillance system to detect a given
## disease in your country. If the probability of disease introduction per
## unit time is 0.10, what surveillance system sensitivity do you need to
## be 95% certain that disease is absent based on the testing carried out as
## part of your program?

## Generate a vector of candidate surveillance system sensitivity estimates
## from 0.1 to 0.99:

se.p <- seq(from = 0.10, to = 0.99, by = 0.01)

## Calculate the probability of disease freedom for each of the candidate
## surveillance system sensitivity estimates:

rval.df <- rsu.pfree.equ(se.p = se.p, p.intro = 0.10)
rval.df <- data.frame(se.p = se.p, depfree = rval.df$depfree)
head(rval.df)

## Which of the surveillance system sensitivity estimates returns a
## probability of freedom greater than 0.95?

rsep.p <- rval.df$se.p[rval.df$depfree > 0.95]
rsep.p[1]

## The required surveillance system sensitivity for this program is 0.69.
## Plot the results:

## Not run:
library(ggplot2)

ggplot(data = rval.df, aes(x = se.p, y = depfree)) +
```

```
   geom_point() +
   geom_line() +
   scale_x_continuous(limits = c(0,1),
      name = "Surveillance system sensitivity") +
   scale_y_continuous(limits = c(0,1),
      name = "Equilibrium discounted probability of disease freedom") +
  geom_hline(aes(yintercept = 0.95), linetype = "dashed") +
  geom_vline(aes(xintercept = rsep.p[1]), linetype = "dashed") +
   theme_bw()

## End(Not run)
```

`rsu.pfree.rs` *Calculate the probability of freedom for given population sensitivity and probability of introduction*

Description

Calculates the posterior probability (confidence) of disease freedom (negative predictive value) for one or more population sensitivity (se.p) estimates, over one or more time periods.

Usage

```
rsu.pfree.rs(se.p, p.intro = 0, prior = 0.5, by.time = TRUE)
```

Arguments

`se.p`	scalar, vector or matrix representing the population sensitivity estimates. `se.p` will be scalar if you're calculating the posterior probability of disease freedom for a single time period. If `se.p` is a vector set `by.time = TRUE` if the `se.p` estimates are for separate time periods. Set `by.time = FALSE` if the `se.p` estimates are variations (iterations) within a single time period. If `se.p` is a matrix, columns represent consecutive time periods and rows represent multiple `se.p` estimates per time period.
`p.intro`	scalar, vector or matrix representing the probability of disease introduction per time period. If `p.intro` is scalar this value is applied across all `se.p` values and time periods. If `p.intro` is a vector set `by.time = TRUE` if the `p.intro` estimates are for separate time periods. Set `by.time = FALSE` if the `p.intro` estimates are variations (iterations) within a single time period. If `p.intro` is a matrix it should have the same dimensions as `se.p` with columns representing time periods and rows representing multiple `p.intro` estimates per time period.
`prior`	scalar or vector of the same length as the number of rows of `se.p` representing the prior probability of disease freedom before surveillance.
`by.time`	logical, representing the type of analysis. See details, below.

Details

The by.time argument is used for two specific circumstances.

Use by.time = TRUE if the se.p estimates are a vector of values for consecutive time periods. Use by.time = FALSE if the se.p estimates are a vector of multiple values (iterations) for a single time period.

Use by.times = TRUE if se.p is a symmetrical matrix and p.intro is a vector of values representing the probability of disease introduction over consecutive time periods. Use by.time = FALSE if se.p is a symmetrical matrix (with columns for time periods and rows representing estimates of se.p within each time period) and p.intro is a vector of values corresponding to multiple values for a single time period that are the same across all periods.

Value

A list comprised of six elements:

PFree	The posterior probability of disease freedom.
SeP	The population sensitivity.
PIntro	The probability of disease introduction (as entered by the user).
Discounted prior	The discounted prior confidence of disease freedom.
Equilibrium PFree	The equilibrium probability of disease freedom.
Equilibrium prior	The equilibrium discounted prior probability of disease freedom.

References

Martin P, Cameron A, Greiner M (2007). Demonstrating freedom from disease using multiple complex data sources 1: A new methodology based on scenario trees. Preventive Veterinary Medicine 79: 71 - 97.

Martin P, Cameron A, Barfod K, Sergeant E, Greiner M (2007). Demonstrating freedom from disease using multiple complex data sources 2: Case study - classical swine fever in Denmark. Preventive Veterinary Medicine 79: 98 - 115.

Examples

```
## EXAMPLE 1:
## You have estimated herd-sensitivity for 20 herds for a disease of concern,
## all returned negative results. What is the confidence of disease freedom
## for these herds, assuming that based on other data, 20% of herds in the
## region are estimated to be disease positive?

## Generate 20 herd sensitivity estimates, using random values between 70%
## and 95%:

herd.sens <- runif(n = 20, min = 0.70, max = 0.95)

## The background herd prevalence is 0.20, so the prior confidence of freedom
```

```
## is 1 - 0.2 = 0.8. For this example we assume the prior is applicable at
## the time of sampling so p.intro = 0 (the default) and we are carrying out
## an analysis using multiple estimates of population sensitivities for a
## single time period so we set by.time = FALSE.

rval.df <- rsu.pfree.rs(se.p = herd.sens, p.intro = 0, prior = 0.80,
   by.time = FALSE)
rval.df <- data.frame(SeP = rval.df$SeP, PFree = rval.df$PFree)
range(rval.df$SeP)

## The herd-level probability of disease freedom ranges from about 0.93 to
## 0.99 depending on individual herd level sensitivity values.


## EXAMPLE 2:
## You have analysed 12 months of surveillance data for disease X, to provide
## 12 monthly estimates of population sensitivity. In addition, based on
## previous data, the monthly probability of the introduction of disease is
## estimated to be in the range of 0.005 (0.5%) to 0.02 (2%). The prior
## confidence of disease freedom is assumed to be 0.5 (i.e., uninformed).
## What is your level of confidence of disease freedom at the end of the 12
## month surveillance period?

## Generate 12, monthly estimates of se.p and p.intro:

pop.sens <- runif(n = 12, min = 0.40, max = 0.70)
pintro <- runif(n = 12, min = 0.005, max = 0.020)

## For this example we're analysing a single population over multiple time
## periods, so we set by.time = TRUE:

rval.df <- rsu.pfree.rs(se.p = pop.sens, p.intro = pintro, prior = 0.50,
   by.time = TRUE)
rval.df <- data.frame(mnum = 1:12, mchar = seq(as.Date("2020/1/1"),
   by = "month", length.out = 12), SeP = t(rval.df$SeP),
   PFree = t(rval.df$PFree))

## Plot the probability of disease freedom as a function of time:
plot(x = rval.df$mnum, y = rval.df$PFree, xlim = c(1,12), ylim = c(0,1),
   xlab = "Month", ylab = "Probability of disease freedom",
   pch = 16, type = "b", xaxt = "n")
axis(side = 1, at = rval.df$mnum,
   labels = format(rval.df$mchar, format = "%b"))
abline(h = 0.95, lty = 2)

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

ggplot(data = rval.df, aes(x = mchar, y =PFree)) +
  geom_line(col = "black") +
  scale_x_date(breaks = date_breaks("1 month"), labels = date_format("%b"),
     name = "Month") +
  scale_y_continuous(limits = c(0,1), name = "Probability of disease freedom") +
```

```
  geom_hline(yintercept = 0.95, linetype = "dashed") +
  theme_bw()

## End(Not run)

## The estimated probability of disease freedom (Pfree) increases over time
## from about 0.70 (or less) to >0.99, depending on the actual se.p values
## generated by simulation.


## EXAMPLE 3:
## Extending the above example, instead of a simple deterministic estimate,
## you decide to use simulation to account for uncertainty in the monthly
## se.p and p.intro estimates.

## For simplicity, we generate 1200 random estimates of se.p and coerce them
## into a matrix with 12 columns and 100 rows:

pop.sens <- matrix(runif(n = 1200, min = 0.40, max = 0.70), nrow = 100)

## For p.intro we generate a vector of 100 random values, which will then be
## used across all time periods:

pintro <- runif(n = 100, min = 0.005, max = 0.020)

## For this example, because se.p is a matrix and p.intro is a vector matching
## one of the dimensions of se.p, by.time is ignored:

rval.df <- rsu.pfree.rs(se.p = pop.sens, p.intro = pintro, prior = 0.5,
   by.time = TRUE)

## Calculate 95% confidence intervals for the probability of disease freedom:
rval.df <- apply(rval.df$PFree, FUN = quantile, MARGIN = 2,
   probs = c(0.025,0.5,0.975))
rval.df <- data.frame(mnum = 1:12, mchar = seq(as.Date("2020/1/1"),
   by = "month", length.out = 12), t(rval.df))

## Plot the probability of disease freedom as a function of time. Dashed lines
## show the lower and upper bound of the confidence interval around the
## probability of disease freedom estimates:

plot(x = rval.df$mnum, y = rval.df$X50., xlim = c(1,12), ylim = c(0,1),
   xlab = "Month", ylab = "Probability of disease freedom",
   type = "l", lwd = 2, xaxt = "n")
axis(side = 1, at = rval.df$mnum, labels = format(rval.df$mchar, format = "%b"))
lines(x = rval.df$mnum, y = rval.df$X2.5., type = "l", lty = 2)
lines(x = rval.df$mnum, y = rval.df$X97.5., type = "l", lty = 2)

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

ggplot(data = rval.df, aes(x = mchar, y = X50.)) +
  geom_line(col = "black") +
```

```
  geom_ribbon(aes(ymin = X2.5., ymax = X97.5.), alpha = 0.25) +
  scale_x_date(breaks = date_breaks("1 month"), labels = date_format("%b"),
     name = "Month") +
  scale_y_continuous(limits = c(0,1), name = "Probability of disease freedom") +
  theme_bw()

## End(Not run)

## The median probability of disease freedom increases over time from about
## 0.7 (or less) to >0.99, depending on the actual se.p values generated by
## simulation.
```

`rsu.pstar` *Design prevalence back calculation*

Description

Calculates design prevalence required for given sample size and desired surveillance system (population-level) sensitivity, assuming representative sampling, imperfect test sensitivity and perfect test specificity.

Usage

```
rsu.pstar(N = NA, n, se.p, se.u)
```

Arguments

`N`	scalar or vector, integer representing the population size. Use `NA` if unknown.
`n`	scalar or vector, integer representing the number of units sampled.
`se.p`	scalar or vector of the same length as `n` representing the desired surveillance system (population-level) sensitivity.
`se.u`	scalar or vector of the same length as `n` representing the unit sensitivity.

Value

A vector of design prevalence estimates.

References

MacDiarmid S (1988). Future options for brucellosis surveillance in New Zealand beef herds. New Zealand Veterinary Journal 36: 39 - 42.

Martin S, Shoukri M, Thorburn M (1992). Evaluating the health status of herds based on tests applied to individuals. Preventive Veterinary Medicine 14: 33 - 43.

Examples

```
## EXAMPLE 1:
## In a study to provide evidence that your country is free of a given disease
## a total of 280 individuals are sampled. Assume a desired surveillance system
## sensitivity of 0.95 and an individual unit diagnostic sensitivity of 0.98.
## If all unit tests return a negative result, what is the maximum prevalence
## if disease is actually present in the population (i.e., what is the design
## prevalence)?

rsu.pstar(N = NA, n = 280, se.p = 0.95, se.u = 0.98)

## If 280 individuals are sampled and tested and each returns a negative test
## result we can be 95% confident that the maximum prevalence (if disease is
## actually present in the population) is 0.011.


## EXAMPLE 2:
## In a study to provide evidence disease freedom a total of 30 individuals
## are sampled from a set of cattle herds. Assume cattle herds in the study
## region range from 100 to 5000 cows. As above, assume a desired surveillance
## system sensitivity of 0.95 and an individuals unit diagnostic sensitivity
## of 0.98. If all 30 unit tests return a negative result, what is the expected
## design prevalence for each herd?

round(rsu.pstar(N = c(100,500,1000,5000), n = 30,
   se.p = 0.95, se.u = 0.98), digits = 3)

## The expected herd level design prevalence ranges from 0.086 (for a 100
## cow herd) to 0.102 (for a 5000 cow herd).
```

---

rsu.sep *Probability that the prevalence of disease in a population is less than or equal to a specified design prevalence*

Description

Calculates the probability that the prevalence of disease in a population is less than or equal to a specified design prevalence following return of a specified number of negative test results.

Usage

```
rsu.sep(N, n, pstar, se.u)
```

Arguments

N	scalar or vector, integer representing the population size.
n	scalar or vector, integer representing the number of units sampled.
pstar	scalar or vector of the same length as n representing the desired design prevalence.
se.u	scalar or vector of the same length as n representing the unit sensitivity.

Value

A vector of the estimated probability that the prevalence of disease in the population is less than or equal to the specified design prevalence.

References

MacDiarmid S (1988). Future options for brucellosis surveillance in New Zealand beef herds. New Zealand Veterinary Journal 36: 39 - 42.

Martin S, Shoukri M, Thorburn M (1992). Evaluating the health status of herds based on tests applied to individuals. Preventive Veterinary Medicine 14: 33 - 43.

Examples

```
## EXAMPLE 1:
## The population size in a provincial area is 193,000. In a given two-
## week period 7764 individuals have been tested for COVID-19 using an
## approved PCR test which is believed to have a diagnostic sensitivity of
## 0.85. All individuals have returned a negative result. What is the
## probability that the prevalence of COVID-19 in this population is less
## than or equal to 100 cases per 100,000?

rsu.sep(N = 193000, n = 7764, pstar = 100 / 100000, se.u = 0.85)

## If all of the 7764 individuals returned a negative test we can be more than
## 99% confident that the prevalence of COVID-19 in the province is less
## than 100 per 100,000.


## EXAMPLE 2:
## What is the probability that the prevalence of COVID-19 is less than or
## equal to 10 cases per 100,000?

rsu.sep(N = 193000, n = 7764, pstar = 10 / 100000, se.u = 0.85)

## If all of the 7764 individuals returned a negative test we can be 49%
## confident that the prevalence of COVID-19 in the province is less
## than 10 per 100,000.


## EXAMPLE 3:
## In a population of 1000 individuals 474 have been tested for disease X
## using a test with diagnostic sensitivity of 0.95. If all individuals tested
## have returned a negative result what is the maximum prevalence expected
## if disease is actually present in the population (i.e., what is the design
## prevalence)?

pstar <- rsu.pstar(N = 1000, n = 474, se.p = 0.95, se.u = 0.95)
pstar

## If 474 individuals are tested from a population of 1000 and each returns a
## negative result we can be 95% confident that the maximum prevalence (if
```

```
## disease is actually present in the population) is 0.005.

## Confirm these calculations using function rsu.sep. If 474 individuals out
## of a population of 1000 are tested using a test with diagnostic sensitivity
## 0.95 and all return a negative result how confident can we be that the
## prevalence of disease in this population is 0.005 or less?

rsu.sep(N = 1000, n = 474, pstar = pstar, se.u = 0.95)

## The surveillance system sensitivity is 0.95.
```

`rsu.sep.cens` *Surveillance system sensitivity assuming data from a population census*

Description

Calculates the surveillance system (population-level) sensitivity for disease detection assuming imperfect test sensitivity, perfect test specificity and when every unit in the population is tested (a census).

Usage

```
rsu.sep.cens(d = 1, se.u)
```

Arguments

`d`	scalar integer defining the expected number of infected units in the population (that is, the population size multiplied by the design prevalence).
`se.u`	scalar or vector of numbers between 0 and 1 defining the unit sensitivity of the test.

Value

A vector of surveillance system (population-level) sensitivities.)

Examples

```
## EXAMPLE 1:
## Every animal in a population is to be sampled and tested using a test
## with a diagnostic sensitivity of 0.80. What is the probability that
## disease will be detected if we expect that there are five infected animals
## in the population?

rsu.sep.cens(d = 5, se.u = 0.80)

## The probability that disease will be detected (i.e., the surveillance
## system sensitivity) is 0.99 (i.e., quite high, even though the sensitivity
```

```
## of the test is relatively low).


## EXAMPLE 2:
## Calculate the surveillance system sensitivity assuming every animal in
## populations of size 10, 50, 100, 250 and 500 will be sampled and tested,
## assuming a design prevalence in each population of 0.01 and use of a test
## with a diagnostic sensitivity of 0.92.

rsu.sep.cens(d = ceiling(0.01 * c(10,50,100,250,500)), se.u = 0.92)

## For the populations comprised of 100 animals or less the surveillance
## system sensitivity is 0.92. For the populations comprised of greater than
## or equal to 250 animals the surveillance system sensitivity is greater
## than 0.99.
```

`rsu.sep.pass` *Surveillance system sensitivity assuming passive surveillance and representative sampling within clusters*

Description

Calculates the surveillance system (population-level) sensitivity for detection of disease for a passive surveillance system assuming comprehensive population coverage and sampling of clinical cases within diseased clusters.

Usage

```
rsu.sep.pass(N, n, step.p, pstar.c, p.inf.u, se.u)
```

Arguments

`N`	scalar or vector of length equal to the number of rows in `step.p` representing the population size.
`n`	scalar or vector of length equal to the number of rows in `step.p` representing the number of units tested per cluster.
`step.p`	vector or matrix of detection probabilities (0 to 1) for each step in the detection process. If a vector each value represents a step probability for a single calculation. If a matrix, columns are step probabilities and rows are simulation iterations.
`pstar.c`	scalar (0 to 1) or vector of length equal to the number of rows in `step.p` representing the cluster-level design prevalence.
`p.inf.u`	scalar (0 to 1) or vector of length equal to the number of rows in `step.p` representing the probability of disease in sampled and tested units. This is equivalent to the positive predictive value for a given prior probability of infection.
`se.u`	scalar (0 to 1) or vector of length equal to the number of rows in `step.p`, representing the unit sensitivity.

Value

A list comprised of two elements:

se.p	scalar or vector, the estimated surveillance system (population-level) sensitivity of detection.
se.c	scalar or vector, the estimated cluster-level sensitivity of detection.

If step.p is a vector, scalars are returned. If step.p is a matrix, values are vectors of length equal to the number of rows in step.p.

References

Lyngstad T, Hellberg H, Viljugrein H, Bang Jensen B, Brun E, Sergeant E, Tavornpanich S (2016). Routine clinical inspections in Norwegian marine salmonid sites: A key role in surveillance for freedom from pathogenic viral haemorrhagic septicaemia (VHS). Preventive Veterinary Medicine 124: 85 - 95. DOI: 10.1016/j.prevetmed.2015.12.008.

Examples

```
## EXAMPLE 1:
## A passive surveillance system for disease X operates in your country.
## There are four steps to the diagnostic cascade with detection probabilities
## for each process of 0.10, 0.20, 0.90 and 0.99, respectively. Assuming the
## probability that a unit actually has disease if it is submitted for
## testing is 0.98, the sensitivity of the diagnostic test used at the unit
## level is 0.90, the population is comprised of 1000 clusters (herds),
## five animals from each cluster (herd) are tested and the cluster-level
## design prevalence is 0.01, what is the sensitivity of disease detection
## at the cluster (herd) and population level?

rsu.sep.pass(N = 1000, n = 5, step.p = c(0.10,0.20,0.90,0.99),
   pstar.c = 0.01, p.inf.u = 0.98, se.u = 0.90)

## The sensitivity of disease detection at the cluster (herd) level is 0.018.
## The sensitivity of disease detection at the population level is 0.16.
```

---

rsu.sep.rb *Surveillance system sensitivity assuming risk-based sampling and varying unit sensitivity*

Description

Calculates surveillance system (population-level) sensitivity assuming one-stage, risk-based sampling and varying unit sensitivity using either the binomial or hypergeometric methods.

Usage

```
rsu.sep.rb(N, rr, ppr, df, pstar, method = "binomial")
```

Arguments

N	vector of the same length as rr, population size estimates for each risk group.
rr	vector of length equal to the number of risk strata, the relative risk values.
ppr	vector of the same length as rr, population proportions for each risk group.
df	a dataframe of values for each combination of risk stratum and sensitivity level. Column 1 = risk group index, column 2 = unit sensitivities, column 3 = the sample size for risk group and unit sensitivity).
pstar	scalar, the design prevalence.
method	character string indicating the method to be used. Options are binomial or hypergeometric. See details, below.

Details

If method = binomial N is ignored and values for ppr need to be entered. Conversely, if method = hypergeometric, ppr is ignored and calculated from N.

Value

A list comprised of five elements:

sep	scalar, the population-level sensitivity estimate.
epi	vector, effective probability of infection estimates.
adj.risk	vector, adjusted risks.
n	vector, sample size by risk group
se.u	a vector of the mean sensitivity for each risk group.

Examples

```
## EXAMPLE 1:
## Calculate the surveillance system sensitivity assuming one-stage risk-
## based sampling assuming a population comprised of high risk (n = 200
## clusters) and low risk (n = 1800 clusters) where the probability of
## disease in the high risk group is 5 times that of the low risk group.

## Four clusters will be sampled with n = 80, 30, 20 and 30 surveillance
## units within each cluster tested using a test with diagnostic sensitivity
## at the surveillance unit level of 0.92, 0.85, 0.92 and 0.85, respectively.

## Assume a design prevalence of 0.01.

rg <- c(1,1,2,2)
se.u <- c(0.92,0.85,0.92,0.85)
n <- c(80,30,20,30)
df <- data.frame(rg, se.u, n)

rsu.sep.rb(N = c(200,1800), rr = c(5,1), ppr = NA,  df = df, pstar = 0.01,
   method = "hypergeometric")
```

```
## The expected surveillance system sensitivity is 0.993.


## EXAMPLE 2:
## Recalculate, assuming that we don't know the size of the cluster population
## at risk.

## When the size of the cluster population at risk is unknown we set N = NA
## and enter values for ppr (the proportion of the population in each risk
## group). Assume (from above) that 0.10 of the cluster population are in the
## high risk group and 0.90 are in the low risk group.

rsu.sep.rb(N = NA, rr = c(5,1), ppr = c(0.10,0.90), df = df, pstar = 0.01,
   method = "binomial")

## The expected surveillance system sensitivity is 0.980.
```

`rsu.sep.rb1rf` *Surveillance system sensitivity assuming risk-based sampling on one risk factor*

Description

Calculates risk-based surveillance system (population-level) sensitivity with a single risk factor, assuming one-stage risk-based sampling and allowing unit sensitivity to vary among risk strata.

Usage

```
rsu.sep.rb1rf(N, n, rr, ppr, pstar, se.u, method = "binomial")
```

Arguments

`N`	scalar or vector of the same length as that vector of `rr` defining the population size per risk strata. Ignored if `method = "binomial"`.
`n`	scalar or vector of the same length as that vector of `rr` defining the sample size per risk strata.
`rr`	scalar or vector of the same length as that vector of `ppr` defining the relative risk values.
`ppr`	scalar or vector of the same length as that vector of `rr` defining the population proportions in each risk strata. Ignored if `method = "hypergeometric"`.
`pstar`	scalar, defining the design prevalence.
`se.u`	scalar or vector of the same length as that vector of `rr` defining the unit sensitivity (which can vary across strata).
`method`	character string indicating the method to be used. Options are `binomial` or `hypergeometric`. See details, below.

Details

If `method = binomial` `N` is ignored and values for `ppr` need to be entered. Conversely, if `method = hypergeometric`, `ppr` is ignored and calculated from `N`.

Value

A list comprised of two elements:

`se.p`	scalar, surveillance system (population-level) sensitivity estimates.
`epi`	vector, effective probability of infection estimates.
`adj.risk`	vector, adjusted relative risk estimates.

Examples

```
## EXAMPLE 1:
## A cross-sectional study is to be carried out to confirm the absence of
## disease using one-stage risk based sampling. Assume a design prevalence of
## 0.10 at the cluster (herd) level and the total number of clusters in
## the population is unknown. Clusters are categorised as being either high,
## medium or low risk with the probability of disease for clusters in the
## high and medium risk area 5 and 3 times the probability of disease in the
## low risk area. The proportions of clusters in the high, medium and low risk
## area are 0.10, 0.10 and 0.80, respectively and you elect to sample five
## clusters from each of the three areas using a test with diagnostic
## sensitivity of 0.90. What is the surveillance system sensitivity?

rsu.sep.rb1rf(N = NA, n = c(5,5,5), rr = c(5,3,1), ppr = c(0.10,0.10,0.80),
   pstar = 0.10, se.u = 0.90, method = "binomial")

## The surveillance system sensitivity is 0.94.


## EXAMPLE 2:
## Same scenario as above, but this time assume we know how many clusters are
## in the high, medium and low risk areas: 10, 10 and 80, respectively. What is
## the surveillance system sensitivity?

rsu.sep.rb1rf(N = c(10,10,80), n = c(5,5,5), rr = c(5,3,1), ppr = NA,
   pstar = 0.10, se.u = 0.90, method = "hypergeometric")

## The surveillance system sensitivity is 0.96, almost identical to that
## calculated above where the binomial distribution was used to account for
## not knowing the size of the cluster population at risk.
```

`rsu.sep.rb2rf` *Surveillance system sensitivity assuming risk-based sampling on two risk factors*

Description

Calculates risk-based surveillance system (population-level) sensitivity with a two risk factors, assuming [one-stage] risk-based sampling and allowing unit sensitivity to vary among risk strata.

Usage

```
rsu.sep.rb2rf(N, n, rr1, ppr1, rr2, ppr2, pstar, se.u, method = "binomial")
```

Arguments

`N`	matrix of population sizes for each risk group. Rows = levels of `rr1`, columns = levels of `rr2`.
`n`	matrix of the number of surveillance units tested in each risk group. Rows = levels of `rr1`, columns = levels of `rr2`.
`rr1`	scalar or vector defining the first set of relative risk values.
`ppr1`	scalar or vector of the same length as that vector of `rr1` defining the population proportions in each of the first risk strata. Proportions must sum to one. Ignored if `method = "hypergeometric"`.
`rr2`	matrix defining the relative risks for the second risk factor. Rows = levels of `rr1`, columns = levels of `rr2`.
`ppr2`	matrix defining the population proportions in each of the second risk strata. Row proportions must sum to one. Rows = levels of `rr1`, columns = levels of `rr2`. Ignored if `method = "hypergeometric"`.
`pstar`	scalar, defining the design prevalence.
`se.u`	scalar or vector of the same length as that vector of `rr1` defining the unit sensitivity (which can vary across strata).
`method`	character string indicating the method to be used. Options are `binomial` or `hypergeometric`. See details, below.

Details

If `method = binomial` `N` is ignored and values for `ppr` need to be entered. Conversely, if `method = hypergeometric`, `ppr` is ignored and calculated from `N`.

Value

A list comprised of two elements:

`se.p`	scalar, surveillance system (population-level) sensitivity estimates.
`epi`	vector, effective probability of infection estimates.
`adj.risk1`	vector, adjusted relative risk estimates for the first risk factor.
`adj.risk2`	vector, adjusted relative risk estimates for the second risk factor.

Examples

```
## EXAMPLE 1:
## A cross-sectional study is to be carried out to confirm the absence of
## disease using risk based sampling. Assume a design prevalence of 0.01
## at the surveillance unit level. Surveillance units are categorised as
## being either high or low risk with the probability of disease for
## high risk surveillance units 3 times the probability of disease for low
## risk units. The proportion of units in each risk group is 0.20 and 0.80,
## respectively.

## Within each of the two risk categories the probability of disease varies
## with age with younger age groups having four times the risk of disease
## as older age groups. In the high risk area 10% of the population are young
## and 90% are old. In the low risk area 30% of the population are young and
## 70% are old.

## The total number of surveillance units in the population is unknown. The
## numbers of young and old surveillance units tested in the high and low risk
## groups are 40, 20, 20 and 10, respectively. You intend to use a test with
## diagnostic sensitivity of 0.80. What is the surveillance system sensitivity?

rsu.sep.rb2rf(N = NA, n = rbind(c(40,20), c(20,10)),
   rr1 = c(3,1),
   ppr1 = c(0.20,0.80),
   rr2 = rbind(c(4,1), c(4,1)),
   ppr2 = rbind(c(0.10,0.90), c(0.30,0.70)),
   pstar = 0.01,
   se.u = 0.80, method = "binomial")$se.p

## The surveillance system sensitivity is 0.93.


## EXAMPLE 2:
## This example shows the importance of sampling high risk groups. Take the
## same scenario as above but switch the relative proportions sampled by
## risk group --- taking a greater number of samples from the low risk group
## compared with the high risk group:

rsu.sep.rb2rf(N = NA, n = rbind(c(10,20), c(20,40)),
   rr1 = c(3,1),
   ppr1 = c(0.20,0.80),
   rr2 = rbind(c(4,1), c(4,1)),
   ppr2 = rbind(c(0.10,0.90), c(0.30,0.70)),
   pstar = 0.01,
   se.u = 0.80, method = "binomial")$se.p

## The surveillance system sensitivity is 0.69. Here we've taken exactly the
## same number of samples as Example 1, but there's a substantial decrease
## in surveillance system sensitivity because we've concentrated sampling on
## a low risk group (decreasing our ability to detect disease).
```

`rsu.sep.rb2st` *Surveillance system sensitivity assuming risk based, two-stage sampling*

Description

Calculates the surveillance system sensitivity for detection of disease assuming risk based, two-stage sampling (sampling of clusters and sampling of units within clusters), imperfect test sensitivity and perfect test specificity. The method allows for a single risk factor at each stage.

Usage

```
rsu.sep.rb2st(H = NA, N = NA, n, rr.c, ppr.c, pstar.c, rr.u, ppr.u,
   pstar.u, rg, se.u)
```

Arguments

`H`	scalar, integer representing the total number of clusters in the population. Use `NA` if unknown.
`N`	vector, integer representing the number of surveillance units within each cluster. Use `NA` if unknown.
`n`	vector, integer representing the number of surveillance units tested within each cluster.
`rr.c`	cluster level relative risks (vector of length corresponding to the number of risk strata), use `rr.c = c(1,1)` if a risk factor does not apply.
`ppr.c`	vector listing the cluster level population proportions for each risk category. Use `NA` if there are no cluster level risk factors.
`pstar.c`	scalar, numeric (0 to 1) the cluster-level design prevalence.
`rr.u`	surveillance unit level relative risks (vector of length corresponding to the number of risk strata), use `rr.u = c(1,1)` if a risk factor does not apply.
`ppr.u`	matrix providing the surveillance unit level population proportions for each risk group. One row for each cluster, columns = unit level risk groups, not required if `N` is provided.
`pstar.u`	scalar, numeric (0 to 1) the unit-level design prevalence.
`rg`	vector, listing the risk group (index) for each cluster.
`se.u`	scalar, numeric (0 to 1), representing the sensitivity of the diagnostic test at the individual surveillance unit level.

Value

A list comprised of:

`se.p`	the surveillance system (population-level) sensitivity of detection.
`se.c`	the cluster-level sensitivity of detection.

Examples

```
## EXAMPLE 1:
## You have been asked to provide an assessment of a surveillance program
## for Actinobacillus hyopneumoniae in pigs. It is known that there are
## high risk and low risk areas for A. hypopneumoniae in your country with
## the estimated probability of disease in the high risk area thought to
## be around 3.5 times that of the probability of disease in the low risk area.
## It is known that 10% of the 1784 pig herds in the study area are in the
## high risk area and 90% are in the low risk area.

## The risk of A. hypopneumoniae is dependent on age, with adult pigs around
## five times more likely to be A. hypopneumoniae positive compared with
## younger (grower) pigs.

## Pigs from 20 herds have been sampled: 5 from the low-risk area and 15 from
## the high-risk area. All of the tested pigs were adults: no grower pigs
## were tested.

## The ELISA for A. hypopneumoniae in pigs has a diagnostic sensitivity
## of 0.95.

## What is the surveillance system sensitivity if we assume a design
## prevalence of 1 per 100 at the cluster (herd) level and 5 per 100
## at the surveillance system unit (pig) level?

# There are 1784 herds in the study area:

H <- 1784

# Twenty of the 1784 herds are sampled. Generate 20 herds of varying size:
set.seed(1234)

hsize <- rlnorm(n = 20, meanlog = log(10), sdlog = log(8))
hsize <- round(hsize + 20, digits = 0)

# Generate a matrix listing the number of growers and finishers in each of
## the 20 sampled herds. Anywhere between 80% and 95% of the animals in
## each herd are growers:

set.seed(1234)
pctg <- runif(n = 20, min = 0.80, max = 0.95)
ngrow <- round(pctg * hsize, digits = 0)
nfini <- hsize - ngrow
N <- cbind(ngrow, nfini)

# Generate a matrix listing the number of grower and finisher pigs sampled
## from each herd:

nsgrow <- rep(0, times = 20)
nsfini <- ifelse(nfini <= 15, nfini, 15)
n <- cbind(nsgrow, nsfini)
```

```
# The herd-level design prevalence is 0.01 and the individual pig-level design
## prevalence is 0.05:

pstar.c <- 0.01
pstar.u <- 0.05

# For herds in the high-risk area the probability being A. hyopneumoniae
## positive is 3.5 times that of herds in the low-risk area. Ninety
## percent of herds are in the low risk area and 10% are in the high risk area:

rr.c <- c(1,3.5)
ppr.c <- c(0.9,0.1)

## We've sampled 5 herds from the low risk area and 15 herds from the
## high risk area:

rg <- c(rep(1, times = 5), rep(2, times = 15))

## For finishers the probability being A. hyopneumoniae positive is 5 times
## that of growers:

rr.u <- c(1,5)

## The diagnostic sensitivity of the A. hyopneumoniae ELISA is 0.95:

se.u <- 0.95

rsu.sep.rb2st(H = H, N = N, n = n,
   pstar.c = pstar.c, pstar.u = pstar.u,
   rg = rg, rr.c = rr.c, rr.u = rr.u,
   ppr.c = ppr.c, ppr.u = NA,
   se.u = se.u)

## The estimated surveillance system sensitivity of this program is 0.31.


## EXAMPLE 2:
## Repeat these analyses assuming we don't know the total number of pig herds
## in the population and we have only an estimate of the proportions of
## growers and finishers in each herd.

## Generate a matrix listing the proportion of growers and finishers in each
## of the 20 sampled herds:

ppr.u <- cbind(rep(0.9, times = 20), rep(0.1, times = 20))

# Set H (the number of clusters) and N (the number of surveillance units
## within each cluster) to NA:

rsu.sep.rb2st(H = NA, N = NA, n = n,
   pstar.c = pstar.c, pstar.u = pstar.u,
   rg = rg, rr.c = rr.c, rr.u = rr.u,
   ppr.c = ppr.c, ppr.u = ppr.u,
```

```
   se.u = se.u)

## The estimated surveillance system sensitivity is 0.20.
```

`rsu.sep.rbvarse` *Surveillance system sensitivity assuming risk based sampling and varying unit sensitivity*

Description

Calculates the surveillance system (population-level) sensitivity for detection of disease assuming risk based sampling and varying unit sensitivity.

Usage

```
rsu.sep.rbvarse(N, rr, df, pstar)
```

Arguments

`N`	scalar integer or vector of integers the same length as `rr`, representing the population size. Use `NA` if unknown.
`rr`	relative risk values (vector of values corresponding to the number of risk strata).
`df`	dataframe of values for each combination of risk stratum and sensitivity level, column 1 = risk group index, column 2 = unit sensitivity, column 3 = n (sample size for risk group and unit sensitivity).
`pstar`	scalar representing the design prevalence.

Value

A list comprised of five elements:

`sep`	scalar, the population-level sensitivity estimate.
`epi`	vector, effective probability of infection estimates.
`adj.risk`	vector, adjusted risks.
`n`	vector, sample size by risk group
`se.u`	a vector of the mean sensitivity for each risk group.

References

MacDiarmid S (1988). Future options for brucellosis surveillance in New Zealand beef herds. New Zealand Veterinary Journal 36: 39 - 42.

Martin S, Shoukri M, Thorburn M (1992). Evaluating the health status of herds based on tests applied to individuals. Preventive Veterinary Medicine 14: 33 - 43.

Examples

```
## EXAMPLE 1:
## A study has been carried out to detect Johne's disease in a population of
## cattle. There are two risk groups ('high' and 'low') with the risk of
## disease in the high risk group five times that of the low risk group.
## The number of  animals sampled and unit sensitivity varies by risk group, as
## detailed below. Assume there number of cattle in the high risk and low risk
## group is 200 and 1800, respectively.

## Calculate the surveillance system sensitivity assuming a design prevalence
## of 0.01.

rg <- c(1,1,2,2)
se.u <- c(0.92,0.85,0.92,0.85)
n <- c(80,30,20,30)
df <- data.frame(rg = rg, se.u = se.u, n = n)

rsu.sep.rbvarse(N = c(200,1800), rr = c(5,1), df = df, pstar = 0.01)

## The surveillance system sensitivity is 0.99.
```

---

rsu.sep.rs *Surveillance system sensitivity assuming representative sampling*

Description

Calculates the surveillance system (population-level) sensitivity for detection of disease assuming representative sampling, imperfect test sensitivity and perfect test specificity using the hypergeometric method if N is known and the binomial method if N is unknown.

Usage

```
rsu.sep.rs(N = NA, n, pstar, se.u = 1)
```

Arguments

N	scalar integer or vector of integers the same length as n, representing the population size. Use NA if unknown.
n	scalar integer or vector of integers representing the number of units tested.
pstar	scalar numeric or vector of numbers the same length as n representing the design prevalence. See details, below.
se.u	scalar numeric or vector of numbers the same length as n representing the unit sensitivity.

Value

A vector of surveillance system (population-level) sensitivity estimates.

References

MacDiarmid S (1988). Future options for brucellosis surveillance in New Zealand beef herds. New Zealand Veterinary Journal 36: 39 - 42.

Martin S, Shoukri M, Thorburn M (1992). Evaluating the health status of herds based on tests applied to individuals. Preventive Veterinary Medicine 14: 33 - 43.

Examples

```
## EXAMPLE 1:
## Three hundred samples are to be tested from a population of animals to
## confirm the absence of a disease. The total size of the population is
## unknown. Assuming a design prevalence of 0.01 and a test with
## diagnostic sensitivity of 0.95 will be used what is the sensitivity of
## disease detection at the population level?

rsu.sep.rs(N = NA, n = 300, pstar = 0.01, se.u = 0.95)

## The sensitivity of disease detection at the population level is 0.943.


## EXAMPLE 2:
## Thirty animals from five herds ranging in size from 80 to 100 head are to be
## sampled to confirm the absence of a disease. Assuming a design prevalence
## of 0.01 and a test with diagnostic sensitivity of 0.95 will be used, what
## is the sensitivity of disease detection for each herd?

N <- seq(from = 80, to = 100, by = 5)
n <- rep(30, times = length(N))
rsu.sep.rs(N = N, n = n, pstar = 0.01, se.u = 0.95)

## The sensitivity of disease detection for each herd ranges from 0.28 to
## 0.36.
```

---

rsu.sep.rs2st — *Surveillance system sensitivity assuming representative two-stage sampling*

Description

Calculates the surveillance system sensitivity for detection of disease assuming two-stage sampling (sampling of clusters and sampling of units within clusters), imperfect test sensitivity and perfect test specificity.

Usage

```
rsu.sep.rs2st(H = NA, N = NA, n, pstar.c, pstar.u, se.u = 1)
```

Arguments

H	scalar, integer representing the total number of clusters in the population. Use NA if unknown.
N	vector, integer representing the number of units within each cluster. Use NA if unknown.
n	vector, integer representing the number of units tested within each cluster.
pstar.c	scalar, numeric (0 to 1) representing the cluster-level design prevalence.
pstar.u	scalar, numeric (0 to 1) representing the unit-level design prevalence.
se.u	scalar, numeric (0 to 1), representing the sensitivity of the diagnostic test at the individual unit level.

Value

A list comprised of:

se.p	the surveillance system (population-level) sensitivity of detection.
se.c	the cluster-level sensitivity of detection.
se.u	the unit-level sensitivity of detection.
N	the number of units within each cluster, as entered by the user.
n	the number of units tested within each cluster, as entered by the user.

Note

If pstar.c is not a proportion N must be provided and N must be greater than n.

Examples

```
## EXAMPLE 1:
## A study is to be conducted to confirm the absence of enzootic bovine
## leukosis disease in your country. Four herds are to be sampled from a
## population of 500 herds. There are 550, 250, 700 and 200 cows in each of
## the four herds. From each of the four herds 30 animals are to be sampled.
## The design prevalence for this study is set to 0.01 at the herd level
## and if a herd is positive for leukosis the individual animal level
## design prevalence is set to 0.10. Assuming a test with diagnostic
## sensitivity of 0.98 will be used, what is the sensitivity of
## disease detection at the population and cluster (herd) level?

rsu.sep.rs2st(H = 500, N = c(550,250,700,200), n = rep(30, times = 4),
   pstar.c = 0.01, pstar.u = 0.10, se.u = 0.98)

## The population level sensitivity of detection is 0.037. The cluster level
## sensitivity of detection ranges from 0.950 to 0.958.
```

`rsu.sep.rsfreecalc` *Surveillance system sensitivity for detection of disease assuming representative sampling and imperfect test sensitivity and specificity.*

Description

Calculates the surveillance system (population-level) sensitivity for detection of disease assuming representative sampling and imperfect test sensitivity and specificity.

Usage

```
rsu.sep.rsfreecalc(N, n, c = 1, pstar, se.u, sp.u)
```

Arguments

`N`	scalar, integer representing the total number of subjects eligible to be sampled. Use `NA` if unknown.
`n`	scalar, integer representing the total number of subjects sampled.
`c`	scalar, integer representing the cut-point number of positives to classify a cluster as positive. If the number of positives is less than `c` the cluster is negative; if the number of positives is greater than or equal to `c` the cluster is positive.
`pstar`	scalar, numeric, representing the design prevalence, the hypothetical outcome prevalence to be detected. See details, below.
`se.u`	scalar, numeric (0 to 1) representing the diagnostic sensitivity of the test at the unit level.
`sp.u`	scalar, numeric (0 to 1) representing the diagnostic specificity of the test at the unit level.

Details

If a value for `N` is entered surveillance system sensitivity is calculated using the hypergeometric distribution. If `N` is `NA` surveillance system sensitivity is calculated using the binomial distribution.

Value

A scalar representing the surveillance system (population-level) sensitivity.

References

Cameron A, Baldock C (1998a). A new probability formula for surveys to substantiate freedom from disease. Preventive Veterinary Medicine 34: 1 - 17.

Cameron A, Baldock C (1998b). Two-stage sampling in surveys to substantiate freedom from disease. Preventive Veterinary Medicine 34: 19 - 30.

Cameron A (1999). Survey Toolbox for Livestock Diseases — A practical manual and software package for active surveillance of livestock diseases in developing countries. Australian Centre for International Agricultural Research, Canberra, Australia.

Examples

```
## EXAMPLE 1:
## Thirty animals from a herd of 150 are to be tested using a test with
## diagnostic sensitivity 0.90 and specificity 0.98. What is the
## surveillance system sensitivity assuming a design prevalence of 0.10 and
## two or more positive tests will be interpreted as a positive result?

rsu.sep.rsfreecalc(N = 150, n = 30, c = 2, pstar = 0.10,
   se.u = 0.90, sp.u = 0.98)

## If a random sample of 30 animals is taken from a population of 150 and
## a positive test result is defined as two or more individuals returning
## a positive test, the probability of detecting disease if the population is
## diseased at a prevalence of 0.10 is 0.87.


## EXAMPLE 2:
## Repeat these calculations assuming herd size is unknown:

rsu.sep.rsfreecalc(N = NA, n = 30, c = 2, pstar = 0.10,
   se.u = 0.90, sp.u = 0.98)

## If a random sample of 30 animals is taken from a population of unknown size
## and a positive test result is defined as two or more individuals returning
## a positive test, the probability of detecting disease if the population is
## diseased at a prevalence of 0.10 is 0.85.
```

---

rsu.sep.rsmult — *Surveillance system sensitivity by combining multiple surveillance components*

Description

Calculates surveillance system (population-level) sensitivity for multiple components, accounting for lack of independence (overlap) between components.

Usage

```
rsu.sep.rsmult(C = NA, pstar.c, rr, ppr, se.c)
```

Arguments

C	scalar integer or vector of the same length as rr, representing the population sizes (number of clusters) for each risk group.
pstar.c	scalar (0 to 1) representing the cluster level design prevalence.
rr	vector of length equal to the number of risk strata, representing the cluster relative risks.

ppr — vector of the same length as rr representing the cluster level population proportions. Ignored if C is specified.

se.c — surveillance system sensitivity estimates for clusters in each component and corresponding risk group. A list with multiple elements where each element is a dataframe of population sensitivity values from a separate surveillance system component. The first column equals the clusterid, the second column equals the cluster-level risk group index and the third column equals the population sensitivity values.

Value

A list comprised of two elements:

se.p — a matrix (or vector if C is not specified) of population-level (surveillance system) sensitivities (binomial and hypergeometric and adjusted vs unadjusted).

se.component — a matrix of adjusted and unadjusted sensitivities for each component.

Examples

```
## EXAMPLE 1:
## You are working with a population that is comprised of indviduals in
## 'high' and 'low' risk area. There are 300 individuals in the high risk
## area and 1200 individuals in the low risk area. The risk of disease for
## those in the high risk area is assumed to be three times that of the low
## risk area.

C <- c(300,1200)
pstar.c <- 0.01
rr <- c(3,1)

## Generate population sensitivity values for clusters in each component of
## the surveillance system. Each of the three dataframes below lists id,
## rg (risk group) and cse (component sensitivity):

comp1 <- data.frame(id = 1:100,
   rg = c(rep(1,time = 50), rep(2, times = 50)),
   cse = rep(0.5, times = 100))

comp2 <- data.frame(id = seq(from = 2, to = 120, by = 2),
   rg = c(rep(1, times = 25), rep(2, times = 35)),
   cse = runif(n = 60, min = 0.5, max = 0.8))

comp3 <- data.frame(id = seq(from = 5, to = 120, by = 5),
   rg = c(rep(1, times = 10), rep(2, times = 14)),
   cse = runif(n = 24, min = 0.7, max = 1))

# Combine the three components into a list:
se.c <- list(comp1, comp2, comp3)

## What is the overall population-level (surveillance system) sensitivity?
```

```
rsu.sep.rsmult(C = C, pstar.c = pstar.c, rr = rr, ppr = NA, se.c = se.c)

## The overall adjusted system sensitivity (calculated using the binomial
## distribution) is 0.85.


## EXAMPLE 2:
## Assume that you don't know exactly how many individuals are in the high
## and low risk areas but you have a rough estimate that the proportion of
## the population in each area is 0.2 and 0.8, respectively. What is the
## population-level (surveillance system) sensitivity?

ppr <- c(0.20,0.80)

rsu.sep.rsmult(C = NA, pstar.c = pstar.c, rr = rr, ppr = ppr, se.c = se.c)

## The overall adjusted system sensitivity (calculated using the binomial
## distribution) is 0.85.
```

`rsu.sep.rspool` *Surveillance system sensitivity assuming representative sampling, imperfect pooled sensitivity and perfect pooled specificity*

Description

Calculates the surveillance system (population-level) sensitivity and specificity for detection of disease assuming representative sampling and allowing for imperfect sensitivity and specificity of the pooled test.

Usage

```
rsu.sep.rspool(r, k, pstar, pse, psp = 1)
```

Arguments

`r`	scalar or vector representing the number of pools.
`k`	scalar or vector of the same length as `r` representing the number of individual units that contribute to each pool (i.e., the pool size).
`pstar`	scalar or vector of the same length as `r` representing the design prevalence.
`pse`	scalar or vector of the same length as `r` representing the pool-level sensitivity.
`psp`	scalar or vector of the same length as `r` representing the pool-level specificity.

Value

A list comprised of two elements:

`se.p`	scalar or vector, the surveillance system (population-level) sensitivity estimates.
`sp.p`	scalar or vector, the surveillance system (population-level) specificity estimates.

References

Christensen J, Gardner I (2000). Herd-level interpretation of test results for epidemiologic studies of animal diseases. Preventive Veterinary Medicine 45: 83 - 106.

Examples

```
## EXAMPLE 1:
## To confirm your country's disease freedom status you intend to use a test
## applied at the herd level. The test is expensive so you decide to pool the
## samples taken from individual herds. If you decide to collect 60 pools,
## each comprised of samples from five herds what is the sensitivity of
## disease detection assuming a design prevalence of 0.01 and the sensitivity
## and specificity of the pooled test equals 1.0?

rsu.sep.rspool(r = 60, k = 5, pstar = 0.01, pse = 1, psp = 1)

## This testing regime returns a population-level sensitivity of disease
## detection of 0.95.


## EXAMPLE 2:
## Repeat these calculations assuming the sensitivity of the pooled test
## equals 0.90.

rsu.sep.rspool(r = 60, k = 5, pstar = 0.01, pse = 0.90, psp = 1)

## If the sensitivity of the pooled test equals 0.90 the population-level
## sensitivity of disease detection is 0.93. How can we improve population-
## level sensitivity? Answer: include more pools in the study.

rsu.sep.rspool(r = 70, k = 5, pstar = 0.01, pse = 0.90, psp = 1)

## Testing 70 pools, each comprised of samples from 5 herds returns a
## population-level sensitivity of disease detection of 0.95.
```

---

rsu.sep.rsvarse — *Surveillance system sensitivity assuming representative sampling and varying unit sensitivity*

Description

Calculates the surveillance system (population-level) sensitivity for detection of disease assuming representative sampling and varying unit sensitivity.

Usage

```
rsu.sep.rsvarse(N = NA, pstar, se.u)
```

Arguments

N	scalar integer or vector of integers the same length as se.u, representing the population size. Use NA if unknown.
pstar	scalar representing the design prevalence.
se.u	vector of numbers the same length as N representing the individual unit sensitivities.

Value

A vector of surveillance system (population-level) sensitivity estimates.

References

MacDiarmid S (1988). Future options for brucellosis surveillance in New Zealand beef herds. New Zealand Veterinary Journal 36: 39 - 42.

Martin S, Shoukri M, Thorburn M (1992). Evaluating the health status of herds based on tests applied to individuals. Preventive Veterinary Medicine 14: 33 - 43.

Examples

```
## EXAMPLE 1:
## A study has been carried out to detect Johne's disease in a population of
## cattle. A random sample of 50 herds from a herd population of unknown size
## has been selected and, from each selected herd, a variable number of animals
## have been tested using faecal culture which is assumed to have a diagnostic
## sensitivity in the order of 0.60.

## The number of animals tested in each of the 50 herds is:
set.seed(1234)
ntest <- round(runif(n = 50, min = 10, max = 30), digits = 0)
ntest

## Calculate the herd level sensitivity of disease detection, assuming we've
## been provided with no details of the number of animals in each of the 50
## herds. Assume a within-herd design prevalence of 0.05:

herd.se <- rsu.sep.rs(N = NA, n = ntest, pstar = 0.05, se.u = 0.60)
range(herd.se)

## The herd level sensitivity of detection varies between 0.26 and 0.60.

## Calculate the surveillance system sensitivity assuming a herd-level design
## prevalence of 0.01:

rsu.sep.rsvarse(N = NA, pstar = 0.01, se.u = herd.se)

## The surveillance system sensitivity is 0.20.
```

`rsu.spp.rs` *Surveillance system specificity assuming representative sampling*

Description

Calculates surveillance system (population level) specificity assuming representative sampling and imperfect test specificity.

Usage

```
rsu.spp.rs(N, n, c = 1, sp.u)
```

Arguments

`N`	scalar or vector of the same length as that vector of `n` defining the [cluster] population size. Use `NA` if the size of the population not known, or for a more general application see details, below.
`n`	scalar or vector defining the sample size.
`c`	scalar or vector of the same length as that vector of `n` defining the cut-point number of positives to classify a cluster as positive, if the number of positive samples is less than `c` the cluster is declared is negative, if the number of positive samples is greater than `c` the cluster is declared positive.
`sp.u`	scalar (0 to 1) or vector of same length as `n`, the specificity of the diagnostic test at the surveillance unit level.

Details

This function calculates population specificity using the hypergeometric distribution if `N` and `c` are provided and the binomial distribution otherwise.

If `N` is provided the number of false positives is fixed, based on `N` and test specificity `sp.u`. This implies that test specificity is a fixed individual-level characteristic (e.g., due to specific cross-reacting infection). If `N` is not supplied, cluster (e.g., herd) specificity is a random binomial function based only on the number of samples and test specificity (i.e., specificity is a function of the test and independent of individual characteristics).

Value

A vector of population specificity estimates.

References

Martin S, Shoukri M, Thorburn M (1992). Evaluating the health status of herds based on tests applied to individuals. Preventive Veterinary Medicine 14: 33 - 43.

Examples

```
## EXAMPLE 1:
## Calculate the surveillance system specificity (i.e., the probability that
## an uninfected population will be correctly identified as negative) if 30
## surveillance units have been tested from a population of 150 using a
## diagnostic test with surveillance unit specificity of 0.90, using a
## cut-point of one or more positives to consider the population positive.

## A specificity of 0.90 means that 9 out of 10 samples from disease-negative
## surveillance units will return a negative result (i.e., one of them will be
## a false positive).

rsu.spp.rs(N = 150, n = 30, c = 1, sp.u = 0.90)

## The surveillance system specificity is 0.03. There is a probability of
## 0.03 that all 30 samples will be negative.


## EXAMPLE 2:
## Now assume we set a cut-point of 6. That is, 6 or more samples have to
## return a positive result for us to declare the population positive:

rsu.spp.rs(N = 150, n = 30, c = 6, sp.u = 0.90)

## The surveillance system specificity is 0.95.
```

---

rsu.sspfree.rs *Sample size to achieve a desired probability of disease freedom assuming representative sampling*

Description

Calculates the required sample size to achieve a desired (posterior) probability of disease freedom assuming representative sampling, imperfect test sensitivity and perfect test specificity.

Usage

```
rsu.sspfree.rs(N = NA, prior, p.intro, pstar, pfree, se.u)
```

Arguments

N	scalar integer or vector of integers the same length as n, representing the population size. Use NA if unknown.
prior	scalar probability (0 to 1), representing the prior probability that the population is free of disease.
p.intro	scalar or vector of the same length as pfree, representing the probability of disease introduction during the next time period.

pstar	scalar numeric or vector of numbers the same length as pfree representing the design prevalence.
pfree	scalar numeric or vector of numbers the same length as pfree representing the desired probability of disease freedom.
se.u	scalar (0 to 1) representing the sensitivity of the diagnostic test at the surveillance unit level.

Value

A list comprised of three elements:

n	a vector listing the required sample sizes.
sep	a vector listing the population sensitivity estimates.
adj.prior	a vector listing the adjusted priors.

Note

This function returns the sample size to achieve a desired (posterior) probability of disease freedom. Function rsu.sssep.rs returns the sample size to achieve a desired surveillance system sensitivity.

References

Martin P, Cameron A, Greiner M (2007). Demonstrating freedom from disease using multiple complex data sources 1: A new methodology based on scenario trees. Preventive Veterinary Medicine 79: 71 - 97.

Martin P, Cameron A, Barfod K, Sergeant E, Greiner M (2007). Demonstrating freedom from disease using multiple complex data sources 2: Case study - Classical swine fever in Denmark. Preventive Veterinary Medicine 79: 98 - 115.

Examples

```
## EXAMPLE 1:
## Prior surveillance activities and expert opinion lead you to believe that
## there's a 75% chance that your country is free of disease X. To confirm
## your country's disease freedom status you intend to use a test at the herd
## level which has a diagnostic sensitivity of 0.95. The probability of
## disease introduction during the time period of interest is relatively
## low, say 0.01. How many herds need to be sampled to be 95% confident
## that the country is free of disease X assuming a design prevalence of
## 0.01?

rsu.sspfree.rs(N = NA, prior = 0.75, p.intro = 0.01, pstar = 0.01,
   pfree = 0.95, se.u = 0.95)

## A total of 198 herds need to be sampled to meet the requirements of the
## study.
```

`rsu.sssep.rb2st1rf` *Sample size to achieve a desired surveillance system sensitivity assuming risk-based 2-stage sampling on one risk factor at the cluster level*

Description

Calculates the sample size to achieve a desired surveillance system sensitivity assuming risk-based 2-stage sampling on one risk factor at the cluster level, imperfect test sensitivity and perfect test specificity.

Usage

```
rsu.sssep.rb2st1rf(rr, ppr, spr, pstar.c, se.c, pstar.u, se.u, se.p)
```

Arguments

`rr`	vector, defining the relative risk values for each strata in the population.
`ppr`	vector of length `rr` defining the population proportions in each strata.
`spr`	vector of length `rr` defining the planned number of units to be sampled from each strata.
`pstar.c`	scalar (either a proportion or integer) defining the cluster level design prevalence.
`se.c`	scalar proportion, defining the desired cluster level sensitivity.
`pstar.u`	scalar (either a proportion or integer) defining the surveillance unit level design prevalence.
`se.u`	scalar (0 to 1) representing the sensitivity of the diagnostic test at the surveillance unit level.
`se.p`	scalar (0 to 1) representing the desired surveillance system (population-level) sensitivity.

Value

A list comprised of seven elements:

`n.clusters`	scalar, the total number of clusters to be sampled.
`n.clusters.per.strata`	a vector of the same length as `rr` listing the numbers of clusters to be sampled from each risk stratum.
`n.units`	scalar, the total number of units to be sampled.
`n.units.per.strata`	a vector of the same length of `rr` listing the total numbers of units to be sampled from each risk stratum.
`n.units.per.cluster`	scalar, the number of units to be sampled from each cluster.

epinf	a vector of the same length of rr listing the effective probability of infection for each risk stratum.
adj.risk	a vector of the same length of rr listing the adjusted risk values for each risk stratum.

Examples

```
## EXAMPLE 1:
## A cross-sectional study is to be carried out to confirm the absence of
## disease using risk based sampling. The population of interest is comprised
## of individual sampling units managed within clusters.

## Clusters are stratified into 'high', 'medium' and 'low' risk areas
## where the cluster-level risk of disease in the high risk area compared
## with the low risk area is 5 and the cluster-level risk of disease in
## the medium risk area compared with the low risk area is 3.

## The proportions of the population at risk in the high, medium and low
## risk area are 0.10, 0.20 and 0.70, respectively. The proportion of samples
## taken from the high, medium and low risk areas will be 0.40, 0.40 and
## 0.20, respectively.

## You intend to use a test with diagnostic sensitivity of 0.90 and you'd
## like to take a sufficient number of samples to return a cluster-level
## sensitivity of 0.80 and a population-level (system) sensitivity of 0.95.
## How many units need to be sampled to meet the requirements of the study?

rr <- c(5,3,1)
ppr <- c(0.10,0.20,0.70)
spr <- c(0.40,0.40,0.20)

rsu.sssep.rb2st1rf(rr, ppr, spr, pstar.c = 0.01, se.c = 0.80,
   pstar.u = 0.10, se.u = 0.90, se.p = 0.95)

## A total of 197 clusters needs to be sampled, 79 from the high risk area,
## 79 from the medium risk area and 39 from the low risk area. A total of
## 18 units should be sampled from each cluster, 3546 units in total.
```

---

rsu.sssep.rb2st2rf *Sample size to achieve a desired surveillance system sensitivity assuming risk-based 2-stage sampling on two risk factors at either the cluster level, unit level, or both*

Description

Calculates the sample size to achieve a desired surveillance system sensitivity assuming risk-based 2-stage sampling on two risk factors at either the cluster level, the unit level or both, imperfect test sensitivity and perfect test specificity.

Usage

```
rsu.sssep.rb2st2rf(rr.c, ppr.c, spr.c, pstar.c, se.c,
   rr.u, ppr.u, spr.u, pstar.u, se.u, se.p)
```

Arguments

rr.c	vector, corresponding to the number of risk strata defining the relative risk values at the cluster level.
ppr.c	vector of length equal to that of rr.c defining the population proportions at the cluster level.
spr.c	vector of length equal to that of rr.c defining the planned surveillance proportions at the cluster level.
pstar.c	scalar (either a proportion or integer) defining the cluster level design prevalence.
se.c	scalar (proportion), the desired cluster level sensitivity.
rr.u	vector, corresponding to the number of risk strata defining the relative risk values at the surveillance unit level.
ppr.u	vector, of length equal to that of rr.u defining the population proportions at the surveillance unit level.
spr.u	vector of length equal to that of rr.u defining the planned surveillance proportions at the surveillance unit level.
pstar.u	scalar (either a proportion or integer) defining the surveillance unit level design prevalence.
se.u	scalar (0 to 1) representing the sensitivity of the diagnostic test at the surveillance unit level.
se.p	scalar (0 to 1) representing the desired surveillance system (population-level) sensitivity..

Value

A list comprised of two elements:

clusters	scalar, the total number of clusters to be sampled.
units	scalar, the total number of units to sample from each cluster.

Examples

```
## EXAMPLE 1:
## A cross-sectional study is to be carried out to confirm the absence of
## disease using risk based sampling. Assume a design prevalence of 0.02
## at the cluster (herd) level and a design prevalence of 0.10 at the
## surveillance unit (individual) level. Clusters are categorised as
## being either high, medium or low risk with the probability of disease for
## clusters in the high and medium risk area 5 and 3 times the probability of
## disease in the low risk area. The proportions of clusters in the high,
## medium and low risk area are 0.10, 0.20 and 0.70, respectively. The
```

```
## proportion of samples from the high, medium and low risk area will be
## 0.40, 0.40 and 0.20, respectively.

## Surveillance units (individuals) are categorised as being either high or
## low risk with the probability of disease for units in the high risk group
## 4 times the probability of disease in the low risk group. The proportions
## of units in the high and low risk groups are 0.10 and 0.90, respectively.
## All of your samples will be taken from units in the high risk group.

## You intend to use a test with diagnostic sensitivity of 0.95 and you'd
## like to take sufficient samples to be 95% certain that you've detected
## disease at the population level, 95% certain that you've detected disease
## at the cluster level and 95% at the surveillance unit level. How many
## clusters and how many units need to be sampled to meet the requirements
## of the study?

rsu.sssep.rb2st2rf(
   rr.c = c(5,3,1), ppr.c = c(0.1,0.2,0.7), spr.c = c(0.4,0.4,0.2),
   pstar.c = 0.02, se.c = 0.95,
   rr.u = c(4,1), ppr.u = c(0.1, 0.9), spr.u = c(1,0),
   pstar.u = 0.10, se.u = 0.90,
   se.p = 0.95)

## A total of 82 clusters needs to be sampled: 33 from the high risk area,
## 33 from the medium risk area and 16 from the low risk area. A total of
## 10 surveillance units should be sampled from each cluster.
```

`rsu.sssep.rbmrg` *Sample size to achieve a desired surveillance system sensitivity assuming risk-based sampling and multiple sensitivity values within risk groups*

Description

Sample the size to achieve a desired population sensitivity assuming risk-based sampling, multiple sensitivity values within risk groups for each risk group and perfect test specificity.

Usage

```
rsu.sssep.rbmrg(pstar, rr, ppr, spr, spr.rg, se.p, se.u)
```

Arguments

`pstar`	scalar, the design prevalence.
`rr`	vector of length equal to the number of risk strata, the relative risk values.
`ppr`	vector of the same length as `rr`, population proportions for each risk group.
`spr`	vector of the same length as `rr`, the planned surveillance proportions for each risk group.

spr.rg	matrix with rows equal to the number of risk groups and columns equal to the number of sensitivity values (row sums must equal 1), the proportions of samples for each sensitivity value in each risk group.
se.p	scalar (0 to 1) representing the desired surveillance system (population-level) sensitivity.
se.u	vector (0 to 1) representing the sensitivity of the diagnostic test at the surveillance unit level.

Value

A list comprised of three elements:

n	matrix of sample sizes for each risk and sensitivity group.
epi	a vector of effective probability of infection estimates.
mean.se	a vector of the mean sensitivity for each risk group.

Examples

```
## EXAMPLE 1:
## You are working with a disease of cattle where the prevalence is believed
## to vary according to herd type. The risk of disease is 5 times greater
## in dairy herds and 3 times greater in mixed herds compared with the
## reference category, beef herds. The distribution of dairy, mixed and beef
## herds in the population of interest is 0.10, 0.10 and 0.80, respectively.
## You intend to distribute your sampling effort 0.4, 0.4 and 0.2 across dairy,
## mixed and beef herds, respectively.

## Within each of the three risk groups a single test with a diagnostic
## sensitivity of 0.95 will be used. How many herds need to be sampled if
## you want to be 95% certain of detecting disease if it is present in the
## population at a prevalence of 1% or greater?

## Generate a matrix listing the proportions of samples for each test in
## each risk group (the number of rows equal the number of risk groups,
## the number of columns equal the number of tests):

m <- rbind(1,1,1)

rsu.sssep.rbmrg(pstar = 0.01, rr = c(5,3,1), ppr = c(0.1,0.1,0.8),
   spr = c(0.4,0.4,0.2), spr.rg = m, se.p = 0.95, se.u = 0.95)

## A total of 147 herds need to be sampled: 59 dairy, 59 mixed and 29
## beef herds.


## EXAMPLE 2:
## Now assume that one of two tests will be used for each herd. The first
## test has a diagnostic sensitivity of 0.92. The second test has a diagnostic
## sensitivity of 0.80. The proportion of dairy, mixed and beef herds receiving
## the first test is 0.80, 0.50 and 0.70, respectively (which means that 0.20,
## 0.50 and 0.30 receive the second test, respectively).
```

```
## Recalculate the sample size.

m <- rbind(c(0.8,0.2), c(0.5,0.5), c(0.7,0.3))

rsu.sssep.rbmrg(pstar = 0.01, rr = c(5,3,1), ppr = c(0.1,0.1,0.8),
   spr = c(0.4,0.4,0.2), spr.rg = m, se.p = 0.95, se.u = c(0.92,0.80))

## A total of 159 herds need to be sampled: 64 dairy, 64 mixed and 31
## beef herds.
```

`rsu.sssep.rbsrg` *Sample size to achieve a desired surveillance system sensitivity assuming risk-based sampling and a single sensitivity value for each risk group*

Description

Sample the size to achieve a desired population sensitivity assuming risk-based sampling, a single sensitivity value for each risk group and perfect test specificity.

Usage

```
rsu.sssep.rbsrg(pstar, rr, ppr, spr, se.p, se.u)
```

Arguments

`pstar`	scalar, representing the design prevalence.
`rr`	vector, defining the relative risk values for each strata in the population.
`ppr`	vector of length `rr`, defining the population proportions in each strata.
`spr`	vector of length `rr` representing the planned surveillance proportion for each strata in the population.
`se.p`	scalar (0 to 1) representing the desired surveillance system (population-level) sensitivity.
`se.u`	scalar (0 to 1) or vector of the same lengthe as `rr` representing the sensitivity of the diagnostic test applied at the unit level.

Value

A list of comprised of four elements:

`n`	a vector listing the required sample sizes for each (risk) strata.
`total`	scalar, representing the total sample size.
`epinf`	a vector listing the effective probability of infection estimates.
`adj.risk`	a vector listing the adjusted risk estimates.

Examples

```
## EXAMPLE 1:
## A cross-sectional study is to be carried out to confirm the absence of
## disease using risk based sampling. Assume a population level design
## prevalence of 0.10 and there are 'high', 'medium' and 'low' risk areas
## where the risk of disease in the high risk area compared with the low risk
## area is 5 and the risk of disease in the medium risk area compared with
## the low risk area is 3. The proportions of the population at risk in the
## high, medium and low risk area are 0.10, 0.10 and 0.80, respectively.
## Half of your samples will be taken from individuals in the high risk area,
# 0.30 from the medium risk area and 0.20 from the low risk area. You intend
## to use a test with diagnostic sensitivity of 0.90 and you'd like to take
## sufficient samples to return a population sensitivity of 0.95. How many
## units need to be sampled to meet the requirements of the study?

rsu.sssep.rbsrg(pstar = 0.10, rr = c(5,3,1), ppr = c(0.10,0.10,0.80),
   spr = c(0.50,0.30,0.20), se.p = 0.95, se.u = 0.90)

## A total of 14 units needs to be sampled to meet the requirements of the
## study: 7 from the high risk area, 4 from the medium risk area and 3 from
## the low risk area.
```

`rsu.sssep.rs` *Sample size to achieve a desired surveillance system sensitivity assuming representative sampling*

Description

Calculates the sample size to achieve a desired surveillance system sensitivity assuming representative sampling for a single risk factor and varying unit sensitivity using the binomial method.

Usage

```
rsu.sssep.rs(N, pstar, se.p = 0.95, se.u)
```

Arguments

`N`	scalar integer or vector of same length as `pstar`, representing the population size.
`pstar`	a scalar or vector of either proportions (0 to 1) or a positive integers representing the design prevalence. If `pstar` is an integer represents the number of positive units in the population, and `N` must be provided.
`se.p`	scalar or vector of same length as `pstar` representing the desired surveillance system (population-level) sensitivity.
`se.u`	scalar (0 to 1) or vector of the same length as `pstar` representing the sensitivity of the diagnostic test at the surveillance unit level.

Value

A vector of required sample sizes.

Note

This function calculates the required sample size using the hypergeometric distribution if N is provided and the binomial distribution otherwise.

This function returns the sample size to achieve a desired surveillance system sensitivity. Function rsu.sspfree.rs returns the sample size to achieve a desired (posterior) probability of disease freedom.

References

MacDiarmid S (1988). Future options for brucellosis surveillance in New Zealand beef herds. New Zealand Veterinary Journal 36: 39 - 42.

Martin S, Shoukri M, Thorburn M (1992). Evaluating the health status of herds based on tests applied to individuals. Preventive Veterinary Medicine 14: 33 - 43.

Examples

```
## EXAMPLE 1:
## You would like to confirm the absence of disease in a single 1000-cow
## dairy herd. You expect the prevalence of disease in the herd to be 0.05.
## You intend to use a single test with a sensitivity of 0.90 and a
## specificity of 1.00. How many herds need to be sampled if you want to
## be 95% certain that the prevalence of brucellosis in dairy herds is
## less than the design prevalence if all tests are negative?

rsu.sssep.rs(N = 1000, pstar = 0.05, se.p = 0.95, se.u = 0.90)

## We need to sample 65 cows.


## EXAMPLE 2:
## You would like to confirm the absence of disease in a study area comprised
## of 5000 herds. If the disease is present you expect the between-herd
## prevalence to be 0.08. You 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. Assuming the two tests are independent,
## how many herds should be sampled to be 95% certain that the disease
## would be detected if it is present in the study area?

## Calculate the sensitivity and specificity of the diagnostic test regime:

se <- matrix(c(0.90,0.95), ncol = 1, byrow = TRUE); se
sp <- matrix(c(0.80,0.85), ncol = 1, byrow = TRUE); sp

test <- rsu.dxtest(se = se, sp = sp, covar.pos = 0 , covar.neg = 0,
   tconf.int = 0.95, method = "exact", interpretation = "parallel",
```

```
   conf.int = 0.95, nsim = 999)

## Interpretation of the two tests in parallel returns a diagnostic sensitivity
## of 0.995 and a diagnostic specificity of 0.680.

## How many herds should be sampled?

rsu.sssep.rs(N = 5000, pstar = 0.08, se.p = 0.95,
   se.u = test$independent$est[1])

## A total of 38 herds need to be tested to be 95% confident that the disease
## is absent from the study area if all return a negative test.


## 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 herds should we sample to be 95% certain that Mycoplasma would
## be detected if it is present if you use a test with perfect sensitivity?

rsu.sssep.rs(N = 200, pstar = 0.20, se.p = 0.95, se.u = 1.00)

## If you test 15 sows and all of them test negative you can be 95%
## confident that the prevalence rate of Mycoplasma in the herd is less than
## 20%.
```

`rsu.sssep.rs2st` *Sample size to achieve a desired surveillance system sensitivity assuming two-stage sampling*

Description

Calculates the required sample size to achieve a desired surveillance system sensitivity assuming two-stage sampling (sampling of clusters and sampling of units within clusters), imperfect test sensitivity and perfect test specificity.

Usage

```
rsu.sssep.rs2st(H = NA, N = NA, pstar.c, se.c, pstar.u, se.u, se.p)
```

Arguments

`H`	scalar, integer representing the total number of clusters in the population. Use `NA` if unknown.
`N`	vector, integer representing the number of units within each cluster. Use `NA` if unknown.
`pstar.c`	scalar, numeric (0 to 1) representing the cluster level design prevalence.

se.c	scalar, numeric (0 to 1) representing the required cluster level sensitivity.
pstar.u	scalar, numeric (0 to 1) representing the surveillance unit level design prevalence.
se.u	scalar (0 to 1) representing the sensitivity of the diagnostic test at the surveillance unit level.
se.p	scalar (0 to 1) representing the desired surveillance system (population-level) sensitivity.

Value

A list comprised of two data frames: `clusters` and `units`. Data frame `clusters` lists:

H	the total number of clusters in the population, as entered by the user.
nsample	the number of clusters to be sampled.

Data frame `units` lists:

N	the number of units within each cluster, as entered by the user.
nsample	the number of units to be sampled.

References

Cameron A, Baldock C (1998). A new probability formula for surveys to substantiate freedom from disease. Preventive Veterinary Medicine 34: 1 - 17.

Cameron A (1999). Survey Toolbox for Livestock Diseases — A practical manual and software package for active surveillance of livestock diseases in developing countries. Australian Centre for International Agricultural Research, Canberra, Australia.

MacDiarmid S (1988). Future options for brucellosis surveillance in New Zealand beef herds. New Zealand Veterinary Journal 36: 39 - 42.

Martin S, Shoukri M, Thorburn M (1992). Evaluating the health status of herds based on tests applied to individuals. Preventive Veterinary Medicine 14: 33 - 43.

Examples

```
## EXAMPLE 1:
## Sampling is to be carried out to support a claim that a country is free
## of bovine brucellosis. We are not certain of the total number of herds
## in the country and we are not certain of the number of cows within each
## herd.

## The design prevalence for this study is set to 0.01 at the herd level and
## if a herd is positive for brucellosis the individual animal level
## design prevalence is set to 0.10. The sensitivity of the diagnostic
## test to be used is 0.95.

## How many herds and how many animals from within each herd
## need to be sampled to be 95% confident of detecting disease at the
## herd and individual animal level?
```

```
rsu.sssep.rs2st(H = NA, N = NA, pstar.c = 0.01, se.c = 0.95,
   pstar.u = 0.10, se.u = 0.95, se.p = 0.95)

## A total of 314 herds need to be sampled, 31 cows from each herd.


## EXAMPLE 2:
## Now lets say we know that there are 500 cattle herds in the country and
## we have the results of a recent livestock census providing counts of the
## number of cattle in each herd. How many herds and how many animals from
## within each herd need to be sampled to be 95% confident of detecting
## disease at the herd and individual animal level?

# Generate a vector of herd sizes. The minimum herd size is 25.

set.seed(1234)
hsize <- ceiling(rlnorm(n = 500, meanlog = 1.5, sdlog = 2)) + 25

nsample <- rsu.sssep.rs2st(H = 500, N = hsize, pstar.c = 0.01, se.c = 0.95,
   pstar.u = 0.10, se.u = 0.95, se.p = 0.95)

nsample$clusters
head(nsample$units)

## A total of 238 of the 500 herds need to be tested. The number of animals
## to sample from the first herd (comprised of 26 animals) is 18.
```

`rsu.sssep.rsfreecalc` *Sample size to achieve a desired surveillance system sensitivity to detect disease at a specified design prevalence assuming representative sampling, imperfect unit sensitivity and specificity*

Description

Calculates the sample size to achieve a desired surveillance system sensitivity to detect disease at a specified design prevalence assuming representative sampling, imperfect unit sensitivity and specificity .

Usage

```
rsu.sssep.rsfreecalc(N, pstar, mse.p, msp.p, se.u, sp.u, method = "hypergeometric",
   max.ss = 32000)
```

Arguments

N	scalar, integer representing the total number of subjects eligible to be sampled.
pstar	scalar, numeric, representing the design prevalence, the hypothetical outcome prevalence to be detected. See details, below.

mse.p	scalar, numeric (0 to 1) representing the desired population level sensitivity. See details, below.
msp.p	scalar, numeric (0 to 1) representing the desired population level specificity. See details, below.
se.u	scalar (0 to 1) representing the sensitivity of the diagnostic test at the surveillance unit level.
sp.u	scalar, numeric (0 to 1) representing the specificity of the diagnostic test at the surveillance unit level.
method	a character string indicating the calculation method to use. Options are binomial or hypergeometric.
max.ss	scalar, integer defining the maximum upper limit for required sample size.

Details

Type I error is the probabilty of rejecting the null hypothesis when in reality it is true. In disease freedom studies this is the situation where you declare a population as disease negative when, in fact, it is actually disease positive. Type I error equals 1 - SeP.

Type II error is the probabilty of accepting the null hypothesis when in reality it is false. In disease freedom studies this is the situation where you declare a population as disease positive when, in fact, it is actually disease negative. Type II error equals 1 - SpP.

Argument pstar can be expressed as either a proportion or integer. Where the input value for pstar is between 0 and 1 the function interprets pstar as a prevalence. Where the input value for pstar is an integer greater than 1 the function interprets pstar as the number of outcome-positive individuals in the population of individuals at risk. A value for design prevalence is then calculated as pstar / N.

Value

A list comprised of two data frames: summary and details. Data frame summary lists:

n	the minimum number of individuals to be sampled.
N	the total number of individuals eligible to be sampled.
c	the cut-point number of positives to achieve the specified surveillance system (population-level) sensitivity and specificity.
pstar	the design prevalence.
p1	the probability that the population has the outcome of interest at the specified design prevalence.
se.p	the calculated population level sensitivity.
sp.p	the calculated population level specificity.

Data frame details lists:

n	the minimum number of individuals to be sampled.
se.p	the calculated population level sensitivity.
sp.p	the calculated population level specificity.

References

Cameron A, Baldock C (1998a). A new probability formula for surveys to substantiate freedom from disease. Preventive Veterinary Medicine 34: 1 - 17.

Cameron A, Baldock C (1998b). Two-stage sampling in surveys to substantiate freedom from disease. Preventive Veterinary Medicine 34: 19 - 30.

Cameron A (1999). Survey Toolbox for Livestock Diseases — A practical manual and software package for active surveillance of livestock diseases in developing countries. Australian Centre for International Agricultural Research, Canberra, Australia.

Examples

```
## EXAMPLE 1:
## A cross-sectional study is to be carried out to confirm the absence of
## brucellosis in dairy herds using a bulk milk tank test assuming a design
## prevalence of 0.05. Assume the total number of dairy herds in your study
## area is 5000 and the bulk milk tank test to be used has a diagnostic
## sensitivity of 0.95 and a specificity of 1.00. How many herds need to be
## sampled to be 95% certain that the prevalence of brucellosis in dairy herds
## is less than the design prevalence if less than a specified number of
## tests return a positive result?

rsu.sssep.rsfreecalc(N = 5000, pstar = 0.05, mse.p = 0.95, msp.p = 0.95,
   se.u = 0.95, sp.u = 0.98, method = "hypergeometric", max.ss = 32000)$summary

## A system sensitivity of 95% is achieved with a total sample size of 194
## herds, assuming a cut-point of 7 or more positive herds are required to
## return a positive survey result.
```

---

rsu.sssep.rspool — *Sample size to achieve a desired surveillance system sensitivity using pooled samples assuming representative sampling*

Description

Calculates the required sample size to achieve a desired surveilance system sensitivity assuming representative sampling, imperfect pooled test sensitivity and imperfect pooled test specificity.

Usage

```
rsu.sssep.rspool(k, pstar, pse, psp, se.p)
```

Arguments

k	scalar or vector of the same length as sep representing the number of individual units that contribute to each pool (i.e., the pool size).
pstar	scalar or vector of the same length as se.p representing the design prevalence.

pse	scalar or vector of the same length as se.p representing the pool-level sensitivity.
psp	scalar or vector of the same length as se.p representing the pool-level specificity.
se.p	scalar or vector (0 to 1) representing the desired surveillance system (population-level) sensitivity.

Value

A vector of required sample sizes.

References

Christensen J, Gardner I (2000). Herd-level interpretation of test results for epidemiologic studies of animal diseases. Preventive Veterinary Medicine 45: 83 - 106.

Examples

```
## EXAMPLE 1:
## To confirm your country's disease freedom status you intend to use a test
## applied at the herd level. The test is expensive so you decide to pool the
## samples taken from individual herds. How many pooled samples of size 5 are
## required to be 95% confident that you will have detected disease if
## 1% of herds are disease-positive? Assume a diagnostic sensitivity and
## specificity of 0.90 and 0.95 for the pooled testing regime.

rsu.sssep.rspool(k = 5, pstar = 0.01, pse = 0.90, psp = 0.95, se.p = 0.95)

## A total of 32 pools (each comprised a samples from 5 herds) need to be
## tested.
```

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