Package ‘averisk’

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Type Package

Title Calculation of Average Population Attributable Fractions and Confidence Intervals

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Maintainer John Ferguson <john.ferguson@nuigalway.ie>

Description Average population attributable fractions are calculated for a set of risk factors (either binary or ordinal valued) for both prospective and case-control designs. Confidence intervals are found by Monte Carlo simulation. The method can be applied to either prospective or case control designs, provided an estimate of disease prevalence is provided. In addition to an exact calculation of AF, an approximate calculation, based on randomly sampling permutations has been implemented to ensure the calculation is computationally tractable when the number of risk factors is large.

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Author John Ferguson [aut, cre]

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_averisk_: Calculation of Average Population Attributable Fractions and Confidence Intervals.

**Description**

Average population attributable fractions are calculated for a set of risk factors (either binary or ordinal valued) for both prospective and case-control designs. Confidence intervals are found by Monte Carlo simulation. The method can be applied to either prospective or case control designs, provided an estimate of disease prevalence is provided. In addition to an exact calculation of AF, an approximate calculation, based on randomly sampling permutations has been implemented to ensure the calculation is computationally tractable when the number of risk factors is large.

**averisk functions**

*getAF*

getAF

_Calculate average attributable fractions_

**Description**

This function calculates average attributable fractions and confidence intervals for discrete risk factors

**Usage**

```r
getAF(f, the.data, ref_cat = NULL, refy = 0, cat_confounders = NULL, 
cont_confounders = NULL, prev = NA, allperm = TRUE, 
nsample_perm = 1000, approx_error = NA, ci = FALSE, conf_level = 0.99, 
nsample_var = 100, correction_factor = TRUE, quantile_int = FALSE, 
sep_est = TRUE, w = NULL)
```

**Arguments**

- `f` A formula object specifying a logistic regression model for the risk factors. See Details for more information.
- `the.data` A dataframe containing the disease indicator, risk factors and possible confounders.
- `ref_cat` A character vector indicating the reference values for each risk factor. Defaults to NULL. In the case that this argument is not specified, the default R assignment for the reference level is used for risk factors coded as character and factor variables (see ?factor) whereas the minimum value is assigned as the reference level for risk factors coded as numeric vectors. Attributable fractions calculate the proportional change in disease prevalence that might be expected if the entire population had the reference value for each risk factor.
refy
Response value that specifies controls. Defaults to 0.

cat_confounders
A character vector indicating categorical variables that need to be adjusted for (excluding risk factors). Defaults to NULL.

cont_confounders
A character vector indicating categorical variables that need to be adjusted for (excluding risk factors). Defaults to NULL.

prev
A proportion specifying the percentage of the population that have the disease. Defaults to NA. NA is appropriate for prospective and survey designs. Prevalence should be specified for case control designs.

allperm
TRUE gives an exact calculation of the sample average fraction. FALSE gives an approximate calculation. Defaults to TRUE.

nsample_perm
How many permutations are used when calculating approximate attributable fractions? (only necessary to specify when allperm=FALSE). If approx_error is specified, then nsample_perm is the number of sampled permutations for the construction of the standard error (if ci=TRUE), but is overridden in the construction of the point estimate.

approx_error
Specifying this option will calculate average fractions using the number of permutations necessary to approximate the true sample average fraction point estimate to within approx_error. Defaults to NA.

ci
Is a confidence interval required? Defaults to FALSE.

conf_level
The confidence level specified as a proportion. i.e. conf_level=0.95 would imply 95 percent confidence. Only necessary to specify when ci=TRUE

nsample_var
The number of monte carlo iterates of the average fraction that are used when calculating the confidence interval. Only necessary to specify when ci=TRUE.

correction_factor
Whether an extra correction term is subtracted from the estimated standard error due to the monte carlo simulated AFs and the point estimate for the AF being based on different numbers of permutations. Defaults to TRUE. (Only necessary to specify when ci=TRUE and allperm=FALSE)

quantile_int
Confidence interval is calculated from empirical quantiles of the monte carlo simulated AFs. Defaults to FALSE. Only necessary to specify when ci=TRUE. See Details for more information.

sep_est
The point estimate of the AF in a separate calculation to the confidence interval. Defaults to TRUE (Only necessary to specify when ci=TRUE)

w
Optional weighting vector for survey data. Defaults to NULL.

Details
The model formula \( f \) is specified using traditional R notation. For instance, in the situation where the binary response is 'y' and there are 3 risk factors: \( x_1, x_2 \) and \( x_3 \), \( f \) would be specified as \( y \sim x_1 + x_2 + x_3 \). Interactions are not permitted in the model. Confounders (either categorical or continuous) are added as separate arguments in character vectors. When a confidence interval is requested, a symmetric interval around the point estimate AF is given by default. In the case that nsample_var is large, a possibly assymmetric interval may instead be requested using quantile_int=TRUE. In this
case, the interval is generated from percentiles of the Monte Carlo simulates of the AF. Since estimating percentiles of a distribution is more difficult than estimating the overall variance, \( n_{sample\_var} \) should be increased if quantile based confidence intervals are desired, and doing so will significantly increase run-time. Quantile based confidence intervals maybe superior to symmetric intervals when the distribution of the simulated AFs is skewed. However, in our experience, the distribution of Monte Carlo simulates is usually relatively symmetric.

**Value**

If \( ci = \text{TRUE} \), a \( 3 \times (K+1) \) matrix, where \( K \) is the number of risk factors. The first row represents the point estimate for the AF, and the second and third rows lower and upper confidence bounds. If \( ci = \text{FALSE} \), a \( (K+1) \)-dimensional vector with the calculated point estimates for the AF is returned.

**Author(s)**

John Ferguson (john.ferguson@nuigalway.ie)

**References**


**Examples**

```r
# the following example is from Eide and Gefeller, 1995
# simulate data

ex_probs <- c(0.0732, 0.2976, 0.1570, 0.01787, 0.1445, 0.1008, 0.06986, 0.0653, 0.03, 0.05766, 0.09680, 0.04194, 0.02741, 0.02194, 0.02474, 0.01031, 0.12410, 0.09537, 0.08408, 0.09509) # P(E|D)
disease_probs <- c(0.36, 0.0621, 0.236, 0.8411, 0.0507, 0.864, 0.1066, 0.1745, 0.1867, 0.2891, 0.0514, 0.0875, 0.0339, 0.0584, 0.0718, 0.1206, 0.1474, 0.2345, 0.2497, 0.3708) # P(D|E)
pe <- ex_probs/disease_probs # marginal P(E)
pe <- pe/sum(pe)
nond_exposure_probs <- (1-disease_probs)*pe # P(E|not D)
nond_exposure_probs <- nond_exposure_probs/sum(nond_exposure_probs)
ex_probs <- ex_probs/sum(ex_probs)
the.mat <- cbind(c(rep(0,10),rep(1,10)),rep(rep(1:5,each=2),2),rep(c(0,1),10))
ncase <- 500
ncontrol <- 500
casemat <- the.mat[sample(1:20,size=ncase,replace=TRUE,prob=ex_probs),]
case_rows <- cbind(rep(1,ncase),casemat)
controlmat <- the.mat[sample(1:20,size=ncontrol,replace=TRUE,prob=nond_exposure_probs),]
control_rows <- cbind(rep(0,ncontrol),controlmat)
the.d <- rbind(case_rows,control_rows)
colnames(the.d) <- c("y","urban.rural","smoking.category","occupational.exposure")

# Just get the estimate (no confidence interval)
getAF(y~urban.rural+smoking.category+occupational.exposure, the.d, prev=0.09)
```
getAF

## find the average fraction and associated monte-carlo calculated 99% confidence
## No need for approximation here. Assume population prevalence is 9 percent.

getAF(y~urban.rural+smoking.category+occupational.exposure, the.d, prev=0.09, ci=TRUE, conf_level=0.99)

## genetic simulation using more risk factors (disease prevalence = 0.01) might be slow.

## Not run:
thevec <- dbinom(0:40, size= 40, prob=0.2, log = FALSE)
bin_fun <- function(beta_0){
  sum(thevec*exp(beta_0+1*(0:40))/(1+exp(beta_0+1*(0:40))))-0.01
}
beta_0 <- uniroot(bin_fun,lower=-8,upper=5)$root
total_risk <- (0.01-exp(beta_0))/(1-exp(beta_0))/0.01
risk_per_snp <- total_risk/20

case_probabilities <- (thevec+exp(beta_0+(0:40)*0.1))/(1+exp(beta_0+(0:40)*0.1))/0.01
control_probabilities <- thevec+1/(1+exp(beta_0+(0:40)*0.1))/0.99

simdata_genetic <- function(ncase, ncontrol){
  numbersnps_case <- sample(0:40, ncase, prob=case_probabilities, replace=TRUE)
  numbersnps_control <- sample(0:40, ncase, prob=control_probabilities, replace=TRUE)
  case_rows <- cbind(rep(1,ncase), matrix(0, nrow=ncase, ncol=20))
  control_rows <- cbind(rep(0,ncase), matrix(0, nrow=ncontrol, ncol=20))
  for(i in 1:ncase){
    if(numbersnps_case[i]>0){
      positions <- sample(1:40,numbersnps_case[i])
      positions <- ceiling(positions/2)
    }
  }
  for(i in 1:ncontrol){
    if(numbersnps_control[i]>0){
      positions <- sample(1:40,numbersnps_control[i])
      positions <- ceiling(positions/2)
      for(j in 1:length(positions)){
        control_rows[i,positions[j]+1]<- control_rows[i,positions[j]+1]+1
      }
    }
  }
  return(rbind(case_rows, control_rows))
}

the.d <- simdata_genetic(ncase=250, ncontrol=250)
colnames(the.d) <- c("y", paste("SNP", 1:20, sep=""))

## Here we just calculate the approximate average fraction
## from 50 permutations and no confidence interval.
## If CI desired add the argument ci=TRUE and nsample_var to the function.
## 50 permutations is chosen for speed. In reality, 1000 maybe needed

thesnp <- paste0("SNP", 1:20, sep="")
(fmla <- as.formula(paste("y ~ " , paste(thesnp, collapse= "+")))})
getAF(fmla, the.d,prev=0.01, allperm=FALSE, nsample_perm=50, ci=FALSE)

## Instead of specifying the number of permutations,
## you can specify an estimated approximation error.
## The approximation error will be within this bound with 95% confidence
## approximation error of 0.01 specified for reasons of speed.
## In reality, you may want to use a smaller value for approx_error.

getAF(fmla, the.d,prev=0.01, allperm=FALSE, approx_error=0.01, ci=FALSE)

## End(Not run)
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