Package 'CoRpower'

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Type Package

Title Computes CoR power and sample size calculations

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Description Computes correlate of risk (CoR) power and sample size calculations as described in Gilbert, Janes, and Huang (2015). Plotting functions are provided for visualizing results.

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Encoding UTF-8

Imports survival, osDesign

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NeedsCompilation no

R topics documented:

`computeN` *Sample Size Calculations for Correlates of Risk*

Description

Calculates projected sample sizes at the design stage for trials assessing biomarkers as correlates of risk (CoRs).

Usage

```
computeN(Nrand, tau, taumax, VEtauToTaumax, VE0toTau, risk0, dropoutRisk,
  propCasesWithS)
```

Arguments

Nrand	Number of participants randomized to vaccine arm
tau	Biomarker sampling timepoint
taumax	End of follow-up time period
VEtauToTaumax	VE between 'tau' and 'taumax'
VE0toTau	VE between 0 and 'tau'
risk0	Placebo-group endpoint risk between 'tau' and 'taumax'
dropoutRisk	Dropout risk between 0 and 'taumax'
propCasesWithS	Proportion of cases with measured S

Details

This function calculates projected sample sizes and includes options to account for dropout and incomplete sample storage. These projected sample sizes can then be used as input values for the computePower function. Calculations use the following assumptions:

1. Failure time T and censoring time C are independent
2. $T|Z = 0$ follows an exponential distribution with rate parameter θ_t and $C|Z = 0$ follows an exponential distribution with rate parameter θ_c
3. RRtauToTaumax $= P(T <= t|T > \tau, Z = 1)/P(T <= t|T > \tau, Z = 0)$ for all t between tau and taumax (this will only approximately hold).

Value

List with the following elements:

- N: the number of subjects in the vaccine group at risk at tau
- nCases: Number of subjects in the vaccine group at-risk at tau with the clinical event (cases) by taumax.
- nControls: Number of subjects in the vaccine group at-risk at tau without the clinical event (controls) by taumax.
- nCasesWithS: Number of subjects in the vaccine group at-risk at tau with the clinical event (cases) by taumax and with the biomarker measured

See Also

computePower

Examples

```
Nrand = 4100
tau = 3.5
taumax = 24
VEtauToTaumax = 0.75
VE0toTau = 0.75/2
risk0 = 0.034
```

```
dropoutRisk = 0.1
propCasesWithS = 1
computeN(Nrand, tau, taumax, VEtauToTaumax, VE0toTau, risk0, dropoutRisk, propCasesWithS)
```

`computePower` *Power Calculations for Assessing Biomarkers as Correlates of Risk (CoRs), Accounting for Measurement Error and Treatment Efficacy*

Description

Performs power calculations for assessing trichotomous, binary, and continuous biomarkers as correlates of risk, accounting for measurement error and treatment efficacy. Methods are described in [Gilbert, Janes, and Huang (2015). "Power/Sample Size Calculations for Assessing Correlates of Risk in Clinical Efficacy Trials."]

Usage

```
computePower(nCases, nControls, nCasesWithS, controlCaseRatio = NULL,
  VEoverall, risk0, VElat0 = seq(0, VEoverall, len = 20),
  VElat1 = rep(VEoverall, 20), VElowest = NULL, Plat0 = 0.2,
  Plat2 = 0.6, P0 = Plat0, P2 = Plat2, PlatVElowest = NULL,
  spec = NULL, FP0 = NULL, sens = NULL, FN2 = NULL, M = 100,
  alpha = 0.05, sigma2obs = 1, rho = 1, biomType = c("continuous",
  "trichotomous", "binary"), cohort = FALSE, p = NULL,
  tpsMethod = c("PL", "ML", "WL"), saveDir = NULL, saveFile = NULL)
```

Arguments

`nCases`	Number of vaccine recipients at-risk at tau with the clinical event by taumax (regardless of whether the biomarker is measured).
`nControls`	Number of vaccine recipients at-risk at tau *without* the clinical event by taumax (regardless of whether the biomarker is measured).
`nCasesWithS`	Number of vaccine recipients at-risk at tau with the clinical event by taumax and with the biomarker measured.
`controlCaseRatio`	Number of controls sampled per case in the vaccine arm.
`VEoverall`	Overall vaccine efficacy.
`risk0`	Placebo-group endpoint rate between time tau and time taumax.
`VElat0`	For trichotomous (or binary) biomarker, grid of VE (vaccine/placebo) values for the lower protected latent subgroup. Each value of `VElat0` corresponds to one unique effect size (RR_t).
`VElat1`	For trichotomous biomarker, grid of VE (vaccine/placebo) values for the medium protected latent subgroup. For binary biomarker, specify as any vector of same length as `VElat0`; value does not affect function output.
`VElowest`	For continuous bioarker, a vector of values corresponding to the lowest possible value of VE. Typical applications will range `VElowest` from 0 to 1 - `RRoverall`.
`Plat0`	For trichotomous (or binary) biomarker, prevalence of lower protected latent subgroup ($P(X = 0)$, where X is the true latent biomarker).

Plat2	For trichotomous (or binary) biomarker, prevalence of higher protected latent subgroup ($P(X = 2)$, where X is the true latent biomarker).
P0	For trichotomous (or binary) biomarker, probability of low biomarker response ($P(S = 0)$, where S is the observed biomarker). If unspecified, this parameter is set to Plat0.
P2	For trichotomous (or binary) biomarker, probability of high biomarker response ($P(S = 2)$, where S is the observed biomarker). If unspecified, this parameter is set to Plat2.
PlatVElowest	For continuous biomarker, proportion of vaccine recipients with the lowest value of VE.
spec	For trichotomous (or binary) biomarker, numeric scalar or vector specifying the specificity ($P(S = 0\|X = 0)$) of the observed biomarker. Default is NULL, which indicates 'approach 2' is to be used.
FP0	For trichotomous (or binary) biomarker, numeric scalar or vector specifying the low false positive rate ($P(S = 2\|X = 0)$) of the observed biomarker. Default is NULL, which indicates 'approach 2' is to be used.
sens	For trichotomous (or binary) biomarker, numeric scalar or vector specifying the sensitivity ($P(S = 2\|X = 2)$) of the observed biomarker. Default is NULL, which indicates 'approach 2' is to be used.
FN2	For trichotomous (or binary) biomarker, numeric scalar or vector specifying the high false negative rate ($P(S = 0\|X = 2)$) of the observed biomarker. Default is NULL, which indicates 'approach 2' is to be used.
M	Number of simulated clinical trials.
alpha	Two-sided Wald test type-I error rate.
sigma2obs	For continuous biomarker, or for trichotomous (or binary) biomarker simulated using 'approach 2', the variance of the observed biomarker.
rho	For continuous biomarker, or for trichotomous (or binary) biomarker simulated using 'approach 2', a numeric scalar or vector specifying the fraction of protection-relevant variability in the observed biomarker. The first element of this vector should be 1, corresponding to the case of no measurement error.
biomType	Type of biomarker that is used. Default is "continuous"; other choices are "trichotomous" and "binary".
cohort	Sampling design to be used. Default is FALSE, specifying case-control sampling design. If TRUE, case-cohort sampling is used.
p	For case-cohort sampling design, probability that a subject will be in the cohort.
tpsMethod	Character denoting method for fitting the logistic regression model. Choose from "PL" for pseudo-likelihood (default), "ML" for maximum likelihood, and "WL" for weighted likelihood.
saveDir	Character denoting the directory that the function output is to be saved in. Default is NULL.
saveFile	Character denoting the name of the file the function output will be saved in. Output will be saved as an .RData file. Default is NULL.

Details

If nCases, nControls, and nCasesWithS are vectors, then rho must be scalar.

To save output in an .RData file, specify the file directory with saveDir and the name of the file with saveFile.

This function asuumes the scenario VElat1 = VEoverall, which yields the formula VEoverall = (Plat0*VElat0 + Pla
For fixed values of Plat0 and Plat2, this links VElat0 to VElat2 by the formula VElat2 = (VEoverall*(Plat0+Plat2)
which is what the function uses to obtain VElat2.

Following Step 7 in section 3.1 in the manuscript, the measurement error in a trichotomous (or binary) biomarker is accounted for in one of two ways: Approach 1 specifies spec, sens, FP0, and FN2 which determine FP1 and FN1 from equations (7) and (8). Vector inputs are acceptable and allows for the evaluation of biomarkers with different levels of measurement error.

Approach 2 specifies sigma2obs and rho; this approach assumes the normal measurement error model (9) in the manuscript. Specifying spec=NULL, sens=NULL, FP0=NULL, and FN2=NULL defaults to approach 2, which is what is used in illustrations in the manuscript.

Parameters independent of biomarker type and sampling design: nCases, nControls, nCasesWithS, VEoverall, risk0, M, alpha, tpsMethod, saveDir, saveFile

Parameters for trichotomous (or binary) biomarker: VElat0, VElat1, Plat0, Plat2, P0, P2, biomType = "trichomous" (or "binary")

- Parameters for Approach 1: sens, spec, FP0, FN2
- Parameters for Approach 2: sigma2obs, rho

Parameters for continuous biomarker: VElowest, PlatVElowest, sigma2obs, rho, biomType = "continuous"

Parameters for case-control sampling design (without-replacement sampling): controlCaseRatio

Parameters for case-cohort sampling design: cohort=TRUE, p

Value

If trichotomous or binary biomarker, list with the following elements:

- power: fraction of simulated trials in which the null hypothesis H_0 (expression (14) of the manuscript) is rejected.
- RRt: CoR relative risk effect size (risk1(2)/risk1(0))
- risk1_2: vaccine-group endpoint risk for high biomarker responses (P(Y=1|X=2))
- risk1_0: vaccine-group endpoint risk for low biomarker responses (P(Y=1|X=0))
- VElat2: grid of VE (vaccine/placebo) among higher protected latent group
- VElat0: grid of VE (vaccine/placebo) among lower protected latent group
- Plat2: prevalence of higher protected
- Plat0: prevalence of lower protected
- P2: probability of high biomarker response
- P0: probability of low biomarker response
- alphaLat: logit(Y=1|s=0)
- betaLat: logit(Y=1|S=2)-logit(Y=1|s=0)
- sens: sensitivity (P(S=2|X=2))
- spec: specificity (P(S=0|X=0))
- FP0: low false positive rate (P(S=2|X=0))
- FN2: high false negative rate (P(S=0|X=2))
- Ncomplete: total number of subjects at risk at tau, excluding dropouts
- nCases: number of observed cases between tau and taumax

- nCasesWithS: number of observed cases between tau and taumax with measured S or S*
- VEoverall: overall VE
- alpha: two-sided Wald test Type 1 error rate
- rho: protection-relevant fraction of the variance of S*
- controlCaseRatio: ratio of controls to cases in case-control sampling design
- risk0: placeb0-group endpoint risk between tau and taumax

If continuous biomarker, list with the following elements:

- power: fraction of simulated trials in which the null hypothesis H_0 (expression (16) of the manuscript) is rejected.
- RRc: CoR relative risk effect size (risk1(s*)/risk1(s*-1))
- betaLat: variable in logistic regression model: logit(risk1lat(x*)) = alphaLat + betaLat x*
- alphaLat: variable in logistic regression model: logit(risk1lat(x*)) = alphaLat + betaLat x*
- PlatVElowest: prevalence of VElowest
- VElowest: lowest VE level for true biomarker X* <= nu
- sigma2obs: variance of observed biomarker S*
- Ncomplete: total number of subjects at risk at tau, excluding dropouts
- nCases: number of observed cases between tau and taumax
- nCasesWithS: number of observed cases between tau and taumax with measured S*
- VEoverall: overall VE
- alpha: two-sided Wald test Type 1 error rate
- rho: protection-relevant fraction of the variance of S*
- controlCaseRatio: ratio of controls to cases in case-control sampling design
- risk0: placeb0-group endpoint risk between tau and taumax

See Also

computeN

Examples

```
## Trichotomous biomarker, Approach 1, varying sens and spec ##
## Specify sens, spec, FP0, FN2
nCases <- 32
nControls <- 1000
nCasesWithS <- 32
controlCaseRatio <- 5
VEoverall <- 0.75
risk0 <- 0.034
VElat0 <- seq(0, VEoverall, len=20)  # 20 data points for the power curve
VElat1 <- rep(VEoverall, 20)
Plat0 <- 0.2
Plat2 <- 0.6
P0 <- Plat0  # different values of P0 can be set
P2 <- Plat2  # different values of P2 can be set
sens <- spec <- c(1, 0.9, 0.8, 0.7)
FP0 <- FN2 <- rep(0, 4)
```

```
M <- 5
alpha <- 0.05
biomType <- "trichotomous"
computePower(nCases=nCases, nControls=nControls, nCasesWithS=nCasesWithS,
             controlCaseRatio=controlCaseRatio, VEoverall=VEoverall, risk0=risk0,
             VElat0=VElat0, VElat1=VElat1, Plat0=Plat0, Plat2=Plat2, P0=P0, P2=P2,
            M=M, alpha=alpha, spec=spec, FP0=FP0, sens=sens, FN2=FN2, biomType=biomType)

## Not run:
## Trichotomous biomarker, Approach 2, varying rho ##
## Specify rho and sigma2obs

nCases <- 32
nControls <- 1000
nCasesWithS <- 32
controlCaseRatio <- 5
VEoverall <- 0.75
risk0 <- 0.034
VElat0 <- seq(0, VEoverall, len=20)
VElat1 <- rep(VEoverall, 20)
Plat0 <- 0.2
Plat2 <- 0.6
P0 <- Plat0
P2 <- Plat2
M <- 5
alpha <- 0.05
sigma2obs <- 1
rho <- c(1, 0.9, 0.7, 0.5)
biomType <- "trichotomous"
computePower(nCases=nCases, nControls=nControls, nCasesWithS=nCasesWithS,
             controlCaseRatio=controlCaseRatio, VEoverall=VEoverall, risk0=risk0,
             VElat0=VElat0, VElat1=VElat1, Plat0=Plat0, Plat2=Plat2, P0=P0, P2=P2,
             M=M, alpha=alpha, sigma2obs=sigma2obs, rho=rho, biomType=biomType)


## Binary biomarker, Approach 2, varying rho ##
## Plat0 + Plat2 = 1

nCases <- 32
nControls <- 1000
nCasesWithS <- 32
controlCaseRatio <- 5
VEoverall <- 0.75
risk0 <- 0.034
VElat0 <- seq(0, VEoverall, len=20)  # 20 data points for the power curve
VElat1 <- rep(0, 20)  # will not be used by function
Plat0 <- 0.2
Plat2 <- 1 - Plat0
P0 <- Plat0
P2 <- Plat2
M <- 5
alpha <- 0.05
sigma2obs <- 1
rho <- c(1, 0.9, 0.7, 0.5)
biomType <- "binary"
computePower(nCases=nCases, nControls=nControls, nCasesWithS=nCasesWithS,
             controlCaseRatio=controlCaseRatio, VEoverall=VEoverall, risk0=risk0,
```

```
            VElat0=VElat0, VElat1=VElat1, Plat0=Plat0, Plat2=Plat2, P0=P0, P2=P2,
            M=M, alpha=alpha, sigma2obs=sigma2obs, rho=rho, biomType=biomType)


## Continuous biomarker, varying rho ##

nCases <- 32
nControls <- 1000
nCasesWithS <- 32
controlCaseRatio <- 5
VEoverall <- 0.75
risk0 <- 0.034
PlatVElowest <- 0.2
VElowest <- seq(0, VEoverall, len=20)
M <- 5
alpha <- 0.05
sigma2obs <- 1
rho <- c(1, 0.9, 0.7, 0.5)
biomType <- "continuous"
computePower(nCases=nCases, nControls=nControls, nCasesWithS=nCasesWithS,
            controlCaseRatio=controlCaseRatio, VEoverall=VEoverall, risk0=risk0,
            PlatVElowest=PlatVElowest, VElowest=VElowest, M=M, alpha=alpha,
            sigma2obs=sigma2obs, rho=rho, biomType=biomType)


## Continuous biomarker, case-cohort sampling design, varying p ##
nCases <- 32
nControls <- 1000
nCasesWithS <- 32
VEoverall <- 0.75
risk0 <- 0.034
PlatVElowest <- 0.2
VElowest <- seq(0, VEoverall, len=20)
M <- 5
alpha <- 0.05
sigma2obs <- 1
rho <- 0.9
biomType <- "continuous"
cohort <- TRUE
p <- 0.01
computePower(nCases=nCases, nControls=nControls, nCasesWithS=nCasesWithS,
         VEoverall=VEoverall, risk0=risk0, PlatVElowest=PlatVElowest, VElowest=VElowest,
        M=M, alpha=alpha, sigma2obs=sigma2obs, rho=rho, biomType=biomType, cohort=cohort, p=p)
p <- 0.02
computePower(nCases=nCases, nControls=nControls, nCasesWithS=nCasesWithS,
         VEoverall=VEoverall, risk0=risk0, PlatVElowest=PlatVElowest, VElowest=VElowest,
        M=M, alpha=alpha, sigma2obs=sigma2obs, rho=rho, biomType=biomType, cohort=cohort, p=p)
p <- 0.03
computePower(nCases=nCases, nControls=nControls, nCasesWithS=nCasesWithS,
         VEoverall=VEoverall, risk0=risk0, PlatVElowest=PlatVElowest, VElowest=VElowest,
        M=M, alpha=alpha, sigma2obs=sigma2obs, rho=rho, biomType=biomType, cohort=cohort, p=p)


## Continuous biomarker, saving output, varying sample sizes ##

nCases <- 32
nControls <- 1000
```

```
nCasesWithS <- 32
controlCaseRatio <- 5
VEoverall <- 0.75
risk0 <- 0.034
PlatVElowest <- 0.2
VElowest <- seq(0, VEoverall, len=20)
M <- 5
alpha <- 0.05
sigma2obs <- 1
rho <- c(1, 0.9, 0.7, 0.5)
biomType <- "continuous"
saveDir <- "~/myDir"
saveFile <- "MyFile"
computePower(nCases=nCases, nCasesWithS=nCasesWithS, nControls=nControls,
             controlCaseRatio=controlCaseRatio, VEoverall=VEoverall, risk0=risk0,
             PlatVElowest=PlatVElowest, VElowest=VElowest, M=M, alpha=alpha,
         sigma2obs=sigma2obs, rho=rho, biomType=biomType, saveDir=saveDir, saveFile=saveFile)

## End(Not run)
```

`plotPowerCont` *Plot Power Curve against CoR Relative Risk for Continuous Biomarkers*

Description

Plots the power to detect a normally distributed CoR in vaccine recipients against different values of the CoR effect size, RRc, which is the relative risk per standard deviation increase for a noise-free biomarker ($\rho = 1$).

Usage

```
plotPowerCont(outComputePower, outDir = NULL, legendText)
```

Arguments

`outComputePower`	List or list of lists containing output from `computePower`, or character vector specifying the file(s) containing `computePower` output.
`outDir`	Character vector specifying path(s) to output file(s), necessary if `outComputePower` is a character vector. Default is `NULL`.
`legendText`	Character vector specifying the entirety of the legend text. Order of the parameter values must match that of the `computePower` input parameters in order for legend labels to be accurate.

Details

The function's plot can be interpreted in conjunction with the output of the `plotVElatCont` function by matching the CoR relative risk in the two plots and examining power compared to VE. This sheds light on the importance of overall VE on power and allows correlates of risk results to be interpreted in terms of potential correlates of efficacy/protection.

Value

Plot displaying power vs. CoR relative risk

See Also

computePower plotVElatCont plotPowerTri

Examples

```
# Example scenario with continuous biomarker, where values of rho are varied

# Set input parameters for computePower function
nCases <- 10
nControls <- 300
nCasesWithS <- 10
controlCaseRatio <- 5
VEoverall <- 0.75
risk0 <- 0.034
PlatVElowest <- 0.2
VElowest <- seq(0, VEoverall, len=5)
M <- 22
alpha <- 0.05
sigma2obs <- 1
rho <- c(1, 0.7, 0.4)
biomType <- "continuous"

# Output from computePower function is stored in an object as a list
pwr <- computePower(nCases=nCases, nCasesWithS=nCasesWithS, nControls=nControls,
                    controlCaseRatio=controlCaseRatio, risk0=risk0, VEoverall=VEoverall,
                    PlatVElowest=PlatVElowest, VElowest=VElowest, M=M, alpha=alpha,
                    sigma2obs=sigma2obs, rho=rho, biomType=biomType)

# Set parameters for plotPowerCont function
# outComputePower is a list containing output from the computePower function
outComputePower <- pwr
legendText <- paste0("rho = ", c(1, 0.7, 0.4))
plotPowerCont(outComputePower=outComputePower, legendText=legendText)

## Not run:
# Output from computePower function is saved in an RData file
computePower(..., saveDir = "myDir", saveFile = "myFile.RData")
# outComputePower is a character string specifying the file containing the computePower output
# outDir is a character string specifying the outComputePower file directory
outComputePower = "myFile"
outDir = "~/myDir"
legendText <- paste0("rho = ", c(1, 0.7, 0.4))
plotPowerCont(outComputePower, outDir=outDir, legendText = legendText)

## End(Not run)
```

plotPowerTri *Plot Power Curve against CoR Relative Risk for Trichotomous or Binary Biomarkers*

Description

Plots the power to detect a trichotomous or binary CoR in vaccine recipients against different values of the CoR effect size, RRt, which is the relative risk in the high biomarker response subgroup versus the low biomarker response subgroup.

Usage

```
plotPowerTri(outComputePower, outDir = NULL, legendText)
```

Arguments

outComputePower	List or list of lists containing output from computePower, or character vector specifying the file(s) containing computePower output.
outDir	Character vector specifying path(s) to output file(s), necessary if outComputePower is a character vector. Default is NULL.
legendText	Character vector specifying the entirety of the legend text. Order of the parameter values must match that of the computePower input parameters in order for legend labels to be accurate.

Details

If multiple levels are specified for the biomarker measurement error input parameters (i.e., for Sens/Spec or rho) in the computePower function, only the first level is used to determine the RR_t values that are plotted on the x-axis.

Value

Plot displaying power vs. CoR relative risk

See Also

computePower plotPowerCont

Examples

```
# Example scenario with trichotomous biomarker, where values of controlCaseRatio are varied

# Set input parameters for computePower function
nCases <- 10
nControls <- 300
nCasesWithS <- 10
controlCaseRatio <- 5
VEoverall <- 0.75
risk0 <- 0.034
VElat0 <- seq(0, VEoverall, len=5)
```

```
VElat1 <- rep(VEoverall, 5)
Plat0 <- P0 <- 0.2
Plat2 <- P2 <- 0.6
sens <- spec <- 0.8
FP0 <- FN2 <- 0
M <- 50
alpha <- 0.05
biomType <- "trichotomous"

# Output from computePower function is stored in an object as a list
pwr1 <- computePower(nCases=nCases, nControls=nControls, nCasesWithS=nCasesWithS,
                     controlCaseRatio=controlCaseRatio, risk0=risk0, VEoverall=VEoverall,
                    Plat0=Plat0, Plat2=Plat2, P0=P0, P2=P2, VElat0=VElat0, VElat1=VElat1,
              M=M, alpha=alpha, spec=spec, FP0=FP0, sens=sens, FN2=FN2, biomType=biomType)

controlCaseRatio <- 3
pwr2 <- computePower(nCases=nCases, nControls=nControls, nCasesWithS=nCasesWithS,
                     controlCaseRatio=controlCaseRatio, risk0=risk0, VEoverall=VEoverall,
                    Plat0=Plat0, Plat2=Plat2, P0=P0, P2=P2, VElat0=VElat0, VElat1=VElat1,
              M=M, alpha=alpha, spec=spec, FP0=FP0, sens=sens, FN2=FN2, biomType=biomType)

controlCaseRatio <- 1
pwr3 <- computePower(nCases=nCases, nControls=nControls, nCasesWithS=nCasesWithS,
                     controlCaseRatio=controlCaseRatio, risk0=risk0, VEoverall=VEoverall,
                    Plat0=Plat0, Plat2=Plat2, P0=P0, P2=P2, VElat0=VElat0, VElat1=VElat1,
              M=M, alpha=alpha, spec=spec, FP0=FP0, sens=sens, FN2=FN2, biomType=biomType)

# Set parameters for plotPowerTri function
# outComputePower is a list of lists containing outputs from the computePower function
outComputePower <- list(pwr1, pwr2, pwr3)
legendText <- paste0("controls:cases = ", c("5:1","3:1","1:1"))
plotPowerTri(outComputePower=outComputePower, legendText=legendText)

## Not run:
# outComputePower is a character vector specifying the files containing computePower output
# outDir is a character vector specifying the outComputePower file directories
outComputePower = c("myFile1", "myFile2", "myFile3")
outDir = rep("~/myDir", 3)
legendText <- paste0("controls:cases = ", c("5:1","3:1","1:1"))
plotPowerTri(outComputePower, outDir=outDir, legendText = legendText)

## End(Not run)
```

`plotRRgradVE` *Plot Ratio of Relative Risks for Higher/Lower Latent Subgroups against CoR Effect Size RR_t for Trichotomous Biomarker*

Description

Plots the ratio of relative risks for the higher and lower latent subgroups ($RRlat2/RRlat0$) versus the CoR relative risk effect size ($RR_t = risk_1(2)/risk_1(0)$).

Usage

```
plotRRgradVE(outComputePower, outDir = NULL, legendText)
```

Arguments

outComputePower	List or list of lists containing output from computePower, or character vector specifying the file(s) containing computePower output.
outDir	Character vector specifying path(s) to output file(s), necessary if outComputePower is a character vector. Default is NULL.
legendText	Character vector specifying the entirety of the legend text. Order of the parameter values must match that of the computePower input parameters in order for legend labels to be accurate.

Details

When ρ is varied, this plot shows how the relationship between the CoR effect size RRt and the ratio of latent relative risks RRlat2/RRlat0 changes for different values of ρ. RRlat2/RRlat0 is a relative vaccine efficacy parameter because RRlat2 = 1 - VElat2 and RRlat0 = 1 - VElat0. When $\rho = 1$, RRt = RRlat2/RRlat0 such that a CoR in the vaccine group is equivalent to the relative vaccine efficacy parameter, whereas for imperfectly measured biomarkers with $\rho < 1$, RRt>RRlat2/RRlat0 and the CoR effect size is closer to the null than the relative vaccine efficacy parameter is.

Note: RRlat2/RRlat0 = $(risk_1^{lat}(2)/risk_0^{lat}(2))/(risk_1^{lat}(0)/risk_0^{lat}(0)) = risk_1^{lat}(2)/risk_1^{lat}(0)$, assuming risk_0 is constant for all s* and x*.

Value

Plot displaying ratio of relative risks vs. CoR relative risk effect size

See Also

computePower plotPowerTri

Examples

```
# Example scenario with trichotomous biomarker, where values of rho are varied

# Set input parameters for computePower function
nCases <- 10
nControls <- 300
nCasesWithS <- 10
controlCaseRatio <- 3
VEoverall <- 0.75
risk0 <- 0.034
VElat0 <- seq(0, VEoverall, len=10)
VElat1 <- rep(VEoverall, 10)
Plat0 <- P0 <- 0.2
Plat2 <- P2 <- 0.6
M <- 20
alpha <- 0.05
sigma2obs <- 1
rho <- c(1, 0.7, 0.4)
biomType <- "trichotomous"

# Output from computePower function is stored in an object as a list
pwr <- computePower(nCases=nCases, nControls=nControls, nCasesWithS=nCasesWithS,
                    controlCaseRatio=controlCaseRatio, risk0=risk0, VEoverall=VEoverall,
```

```
                    Plat0=Plat0, Plat2=Plat2, P0=P0, P2=P2, VElat0=VElat0, VElat1=VElat1,
                     M=M, alpha=alpha, sigma2obs=sigma2obs, rho=rho, biomType=biomType)

# Set parameters for plotPowerCont function
# outComputePower is a list containing output from the computePower function
outComputePower <- pwr
legendText <- paste0("rho = ", c(1, 0.7, 0.4))
plotRRgradVE(outComputePower=outComputePower, legendText=legendText)

## Not run:
# Output from computePower function is saved in an RData file
computePower(..., saveDir = "myDir", saveFile = "myFile.RData")
# outComputePower is a character string specifying the file containing the computePower output
# outDir is a character string specifying the outComputePower file directory
outComputePower = "myFile"
outDir = "~/myDir"
legendText <- paste0("rho = ", c(1, 0.7, 0.4))
plotRRgradVE(outComputePower, outDir=outDir, legendText = legendText)

## End(Not run)
```

`plotVElatCont` *Plot Vaccine Efficacy Curves for Different CoR Relative Risks for Continuous Biomarkers*

Description

Plots the vaccine efficacy (VE) curve for the true biomarker X*=x* for eight different values of the true CoR relative risk, $RR_c(\rho = 1)$, in vaccine recipients and the lowest vaccine efficacy level for the true biomarker, VE_lowest. All curves assume $\rho = 1$, and VE ranges from 0 to 1. The legend is completely determined by the function.

Usage

```
plotVElatCont(outComputePower, outDir = NULL)
```

Arguments

`outComputePower`	List containing output from `computePower`, or character string specifying the file containing `computePower` output. Must be a one list or character string.
`outDir`	Character string specifying path to output file, necessary if `outComputePower` is a character string. Default is `NULL`. Must be one character string; cannot take a character vector.

Details

`computePower` function input parameter `VElowest` must have length >= 8 for all eight scenarios to have unique RRc and VElowest. Otherwise, only `length(VElowest)` unique VE curves will be displayed.

When interpreting the output of the function, the null hypothesis $H_0 : CoRRR_c = 1$ (expression 16 in the manuscript) corresponds to a flat curve where VE(x*) = VE for all x*. Increasing departures

from the null hypothesis correspond to increasingly variable and steep VE curves. The output assumes $risk_0$ is constant for all x* and s* and there is no measurement error ($\rho = 1$), and one can see that when this is the case, an association of the biomarker with infection risk in the vaccine group (a CoR) is equivalent to an association of the biomarker with VE.

The function's plot can also be interpreted in conjunction with the output of the plotPowerCont function by matching the CoR relative risk in the two plots and examining power compared to VE. This sheds light on the importance of overall VE on power and further enables correlates of risk results to be interpreted in terms of potential correlates of efficacy/protection.

Value

Plot displaying VE curves for various CoR relative risk and lowest VE scenarios

See Also

computePower plotPowerCont

Examples

```
# Example scenario with continuous biomarker, where values of rho are varied

# Set input parameters for computePower function
nCases <- 10
nControls <- 300
nCasesWithS <- 10
controlCaseRatio <- 3
VEoverall <- 0.75
risk0 <- 0.034
PlatVElowest <- 0.2
VElowest <- seq(0, VEoverall, len=8)
M <- 13
alpha <- 0.05
sigma2obs <- 1
rho <- c(1, 0.7, 0.4)
biomType <- "continuous"

# Output from computePower function is stored in an object as a list
pwr <- computePower(nCases=nCases, nCasesWithS=nCasesWithS, nControls=nControls,
                    controlCaseRatio=controlCaseRatio, risk0=risk0, VEoverall=VEoverall,
                    PlatVElowest=PlatVElowest, VElowest=VElowest, M=M, alpha=alpha,
                    sigma2obs=sigma2obs, rho=rho, biomType=biomType)

# Set parameters for plotPowerCont function
# outComputePower is a list containing output from the computePower function
outComputePower <- pwr
plotVElatCont(outComputePower=outComputePower)

## Not run:
# Output from computePower function is saved in an RData file
computePower(..., saveDir = "myDir", saveFile = "myFile.RData")
# outComputePower is a character string specifying the file containing the computePower output
# outDir is a character string specifying the outComputePower file directory
outComputePower = "myFile"
outDir = "~/myDir"
plotVElatCont(outComputePower, outDir=outDir)
```

```
## End(Not run)
```

Index