Package 'CoRpower'

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Title Power Calculations for Assessing Correlates of Risk in Clinical Efficacy Trials

Version 1.0.0

BugReports https://github.com/mjuraska/CoRpower/issues

Description Calculates power for assessment of intermediate biomarker responses as correlates of risk in the active treatment group in clinical efficacy trials, as described in Gilbert, Janes, and Huang, Power/Sample Size Calculations for Assessing Correlates of Risk in Clinical Efficacy Trials (2016, Statistics in Medicine). The methods differ from past approaches by accounting for the level of clinical treatment efficacy overall and in biomarker response subgroups, which enables the correlates of risk results to be interpreted in terms of potential correlates of efficacy/protection. The methods also account for inter-individual variability of the observed biomarker response that is not biologically relevant (e.g., due to technical measurement error of the laboratory assay used to measure the biomarker response), which is important because power to detect a specified correlate of risk effect size is heavily affected by the biomarker's measurement error. The methods can be used for a general binary clinical endpoint model with a univariate dichotomous, trichotomous, or continuous biomarker response measured in active treatment recipients at a fixed timepoint after randomization, with either case-cohort Bernoulli sampling or case-control without-replacement sampling of the biomarker (a baseline biomarker is handled as a trivial special case). In a specified two-group trial design, the computeN() function can initially be used for calculating additional requisite design parameters pertaining to the target population of active treatment recipients observed to be at risk at the biomarker sampling timepoint. Subsequently, the power calculation employs an inverse probability weighted logistic regression model fitted by the tps() function in the 'osDesign' package. Power results as well as the relationship between the correlate of risk effect size and treatment efficacy can be visualized using various plotting functions.

URL https://github.com/mjuraska/CoRpower

Depends R (>= 3.5.0)

License GPL-2

Encoding UTF-8

Imports survival, osDesign

RoxygenNote 6.1.0

Suggests knitr, rmarkdown

VignetteBuilder knitr

LazyData true

NeedsCompilation no

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R topics documented:

`computeN` *Estimation of Size and Numbers of Cases and Controls in the Target Population of Active Treatment Recipients At Risk at the Biomarker Sampling Timepoint*

Description

If the power calculation is done at the study design stage, the function estimates the size and numbers of cases and controls in the target population of active treatment recipients observed to be at risk at the biomarker sampling timepoint.

Usage

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

Arguments

`Nrand`	the number of participants randomized to the active treatment group
`tau`	the biomarker sampling timepoint after randomization
`taumax`	the time after randomization marking the end of the follow-up period for the clinical endpoint

VEtauToTaumax	the treatment (vaccine) efficacy level between τ and τ_{max}
VE0toTau	the treatment (vaccine) efficacy between 0 and τ
risk0	the overall placebo-group endpoint risk between τ and τ_{max}
dropoutRisk	the risk of participant dropout between 0 and τ_{max}
propCasesWithS	the proportion of observed cases with a measured biomarker response

Details

The function estimates design parameters that are required as input to computePower. If the power calculation is done after the follow-up was completed, the estimates are replaced by the observed counterparts for use as input parameters in computePower.

The calculations include options to account for participant dropout by specifying dropoutRisk as well as for incomplete sample storage by specifying propCasesWithS.

The estimation procedure considers the standard survival analysis framework with failure and censoring times denoted by T and C, respectively, and makes the following assumptions:

1. T and C are independent.
2. $T|Z = 0$ follows an exponential distribution with rate θ_t and $C|Z = 0$ follows an exponential distribution with rate θ_c
3. $RR_{\tau-\tau_{max}} := P(T <= \tau_{max}|T > \tau, Z = 1)/P(T <= \tau_{max}|T > \tau, Z = 0)$ is assumed to be equal to $P(T <= t|T > \tau, Z = 1)/P(T <= t|T > \tau, Z = 0)$ for all $t \in (\tau, \tau_{max}]$.

Value

A list with the following components:

- N: the total estimated number of active treatment recipients observed to be at risk at τ
- nCases: the estimated number of clinical endpoint cases observed between τ and τ_{max} in the active treatment group
- nControls: the estimated number of controls observed to complete follow-up through τ_{max} endpoint-free in the active treatment group
- nCasesWithS: the estimated number of clinical endpoint cases observed between τ and τ_{max} in the active treatment group with an available biomarker response

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 Intermediate Biomarkers as Correlates of Risk in the Active Treatment Group in Clinical Efficacy Trials, Accounting for Biomarker's Measurement Error and Treatment Efficacy*

Description

Performs a power calculation for assessing a univariate dichotomous, trichotomous, or continuous intermediate biomarker response as a correlate of risk in the active treatment group in a clinical efficacy trial, accounting for the biomarker's measurement error and treatment efficacy. The statistical methods are described in [Gilbert, Janes, and Huang (2016). "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", "dichotomous"), cohort = FALSE, p = NULL,
  tpsMethod = c("PL", "ML", "WL"), saveDir = NULL, saveFile = NULL)
```

Arguments

`nCases`	an integer value specifying the number of clinical endpoint cases observed (or projected) between τ and τ_{max} in the active treatment group (a numeric vector of multiple counts/scenarios is allowed)
`nControls`	an integer value specifying the number of controls observed (or projected) to complete follow-up through τ_{max} endpoint-free in the active treatment group (a numeric vector of multiple counts/scenarios is allowed)
`nCasesWithS`	an integer value specifying the number of clinical endpoint cases observed (or projected) between τ and τ_{max} in the active treatment group with an available biomarker response (a numeric vector of multiple counts/scenarios is allowed)
`controlCaseRatio`	an integer value specifying the number of controls sampled per case for biomarker measurement in the without replacement case-control sampling design
`VEoverall`	a numeric value specifying the overall treatment (vaccine) efficacy between τ and τ_{max}

risk0	a numeric value specifying the overall placebo-group endpoint risk between τ and τ_{max}
VElat0	a numeric vector specifying a grid of treatment (vaccine) efficacy levels in the latent lower protected subgroup for a dichotomous or trichotomous biomarker. Each value of VElat0 corresponds to one unique effect size (RR_t). It typically ranges from VEoverall (H_0) to 0 (maximal H_1 not allowing harm by treatment).
VElat1	a numeric vector specifying a grid of treatment (vaccine) efficacy levels in the latent medium protected subgroup for a trichotomous biomarker (NULL by default for a dichotomous biomarker)
VElowest	a numeric vector specifying a grid of treatment (vaccine) efficacy levels in the latent lowest-efficacy subgroup for a continuous biomarker. It typically ranges from VEoverall (H_0) to 0 (maximal H_1 not allowing harm by treatment).
Plat0	a numeric value specifying the prevalence of the latent lower protected subgroup for a dichotomous or trichotomous biomarker
Plat2	a numeric value specifying the prevalence of the latent higher protected subgroup for a dichotomous or trichotomous biomarker
P0	a numeric value specifying the probability of low biomarker response for a dichotomous or trichotomous biomarker. If unspecified, it is set to Plat0.
P2	a numeric value specifying the probability of high biomarker response for a dichotomous or trichotomous biomarker. If unspecified, it is set to Plat2.
PlatVElowest	a numeric value specifying the prevalence of the latent lowest-efficacy subgroup for a continuous biomarker
spec	a numeric vector specifying the specificity, i.e., the probability of low biomarker response conditional on membership in the lower protected subgroup, of a dichotomous or trichotomous biomarker. Default is NULL, which indicates the use of 'approach 2'.
FP0	a numeric vector specifying the false positive rate, i.e., the probability of high biomarker response conditional on membership in the lower protected subgroup, for a dichotomous or trichotomous biomarker. Default is NULL, which indicates the use of 'approach 2'.
sens	a numeric vector specifying the sensitivity, i.e., the probability of high biomarker response conditional on membership in the higher protected subgroup, for a dichotomous or trichotomous biomarker. Default is NULL, which indicates the use of 'approach 2'.
FN2	a numeric vector specifying the false negative rate, i.e., the probability of low biomarker response conditional on membership in the higher protected subgroup, for a dichotomous or trichotomous biomarker. Default is NULL, which indicates the use of 'approach 2'.
M	an integer value specifying the number of simulated clinical trials
alpha	a numeric value specifying the two-sided Wald test type-I error rate
sigma2obs	a numeric value specifying the variance of the observed continuous biomarker or of the dichotomous or trichotomous biomarker simulated using 'approach 2'
rho	a numeric vector specifying distinct protection-relevant fractions of sigma2obs

biomType	a character string specifying the biomarker type. Default is continuous; other choices are dichotomous and trichotomous.
cohort	a logical value for whether a case-cohort Bernoulli sampling design is to be used. If FALSE (default), the case-control without replacement sampling is used.
p	a numeric value specifying the probability of sampling into the subcohort in the case-cohort design
tpsMethod	a character string specifying the estimation method in the inverse probability weighted logistic regression model fit by the tps function in the osDesign package. The options are PL for pseudo-likelihood (default), ML for maximum likelihood, and WL for weighted likelihood.
saveDir	a character string specifying the path for a directory in which the output is to be saved. If NULL (default), the output is returned only.
saveFile	a character string specifying the name of the .RData file storing the output. If NULL (default), the output is returned only.

Details

If nCases, nControls, and nCasesWithS are vectors (of the same length), then rho must be a scalar.

To save output in an .RData file, both saveDir and saveFile must be specified.

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

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

- 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 a case-control without replacement sampling design: controlCaseRatio

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

Value

If saveFile and saveDir are both specified, the output list (named pwr) is saved as an .RData file; otherwise it is returned only. For a dichotomous or trichotomous biomarker, the output list has the following components:

- power: a matrix of fractions of simulated trials in which the null hypothesis H_0 is rejected. Rows represent calculations for different values of rho, sens, or nCases, depending on which is a vector. Columns represent calculations for the grid of treatment (vaccine) efficacies specified by VElat0 and VElat1.
- RRt: a matrix of correlate-of-risk relative-risk effect sizes. Rows represent different values of rho, sens, or nCases, depending on which is a vector. Columns represent the grid of treatment (vaccine) efficacies specified by VElat0 and VElat1.

- risk1_2: a matrix of conditional endpoint risks given a high biomarker response in the active treatment group. Rows represent different values of rho, sens, or nCases, depending on which is a vector. Columns represent the grid of treatment (vaccine) efficacies specified by VElat0 and VElat1.
- risk1_0: a matrix of conditional endpoint risks given a low biomarker response in the active treatment group. Rows represent different values of rho, sens, or nCases, depending on which is a vector. Columns represent the grid of treatment (vaccine) efficacies specified by VElat0 and VElat1.
- VElat2: a numeric vector specifying a grid of treatment (vaccine) efficacy levels in the latent higher protected subgroup for a dichotomous or trichotomous biomarker
- VElat0: a numeric vector specifying a grid of treatment (vaccine) efficacy levels in the latent lower protected subgroup for a dichotomous or trichotomous biomarker
- Plat2: a numeric value specifying the prevalence of the latent higher protected subgroup for a dichotomous or trichotomous biomarker
- Plat0: a numeric value specifying the prevalence of the latent lower protected subgroup for a dichotomous or trichotomous biomarker
- P2: a numeric value specifying the probability of high biomarker response for a dichotomous or trichotomous biomarker
- P0: a numeric value specifying the probability of low biomarker response for a dichotomous or trichotomous biomarker
- alphaLat: a numeric vector of the log odds of the clinical endpoint in the subgroup of active treatment recipients with the latent $x^* = 0$ (this coefficient estimate applies to a continuous biomarker)
- betaLat: a numeric vector of the log odds ratio of the clinical endpoint comparing two subgroups of active treatment recipients differing in the latent x^* by 1 (this coefficient estimate applies to a continuous biomarker)
- sens: a numeric vector of sensitivities (i.e., the probability of high biomarker response conditional on membership in the higher protected subgroup) of the observed dichotomous or trichotomous biomarker as a function of rho
- spec: a numeric vector of specificities (i.e., the probability of low biomarker response conditional on membership in the lower protected subgroup) of the observed dichotomous or trichotomous biomarker as a function of rho
- FP0: a numeric vector of false positive rates (i.e., the probability of high biomarker response conditional on membership in the lower protected subgroup) of the observed dichotomous or trichotomous biomarker as a function of rho
- FN2: a numeric vector of false negative rates (i.e., the probability of low biomarker response conditional on membership in the higher protected subgroup) of the observed dichotomous or trichotomous biomarker as a function of rho
- Ncomplete: an integer value specifying nCases + nControls, i.e., the number, observed or projected, of active treatment recipients at risk at τ with an observed endpoint or a completed follow-up through τ_{max}
- nCases: an integer value specifying the number of clinical endpoint cases observed (or projected) between τ and τ_{max} in the active treatment group

- nCasesWithS: an integer value specifying the number of clinical endpoint cases observed (or projected) between τ and τ_{max} in the active treatment group with an available biomarker response
- controlCaseRatio: an integer specifying the number of controls sampled per case for biomarker measurement in the without replacement case-control sampling design
- VEoverall: a numeric value specifying the overall treatment (vaccine) efficacy between τ and τ_{max}
- risk0: a numeric value specifying the overall placebo-group endpoint risk between τ and τ_{max}
- alpha: a numeric value specifying the two-sided Wald test type-I error rate
- rho: a numeric vector specifying distinct protection-relevant fractions of the variance of the observed biomarker

For a continuous biomarker, a list with the following components:

- power: a matrix of fractions of simulated trials in which the null hypothesis H_0 is rejected. Rows represent calculations for different values of rho or nCases, depending on which is a vector. Columns represent calculations for the grid of treatment (vaccine) efficacy levels in the latent lowest-efficacy subgroup, specified by VElowest.
- RRc: a numeric vector of correlate-or-risk relative-risk effect sizes as a function of the grid of treatment (vaccine) efficacy levels in the latent lowest-efficacy subgroup, specified by VElowest
- betaLat: a numeric vector specifying the log odds ratio of the clinical endpoint comparing two subgroups of active treatment recipients differing in the latent x^* by 1 (this coefficient estimate applies to a continuous biomarker)
- alphaLat: a numeric vector specifying the the log odds of the clinical endpoint in the subgroup of active treatment recipients with the latent $x^* = 0$ (this coefficient estimate applies to a continuous biomarker)
- PlatVElowest: a numeric value specifying the prevalence of the latent lowest-efficacy subgroup for a continuous biomarker
- VElowest: a numeric vector specifying a grid of treatment (vaccine) efficacy levels in the latent lowest-efficacy subgroup for a continuous biomarker
- sigma2obs: a numeric value specifying the variance of the observed continuous biomarker or of the dichotomous or trichotomous biomarker simulated using 'approach 2'
- Ncomplete: an integer value specifying nCases + nControls, i.e., the number, observed or projected, of active treatment recipients at risk at τ with an observed endpoint or a completed follow-up through τ_{max}
- nCases: an integer value specifying the number of clinical endpoint cases observed (or projected) between τ and τ_{max} in the active treatment group
- nCasesWithS: an integer value specifying the number of clinical endpoint cases observed (or projected) between τ and τ_{max} in the active treatment group with an available biomarker response
- VEoverall: a numeric value specifying the overall treatment (vaccine) efficacy between τ and τ_{max}

- alpha: a numeric value specifying the two-sided Wald test type-I error rate
- rho: a numeric vector specifying distinct protection-relevant fractions of the variance of the observed biomarker
- controlCaseRatio: an integer value specifying the number of controls sampled per case for biomarker measurement in the without replacement case-control sampling design
- risk0: a numeric value specifying the overall placebo-group endpoint risk between τ and τ_{max}

See Also

computeN, plotPowerTri, plotPowerCont

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)


## dichotomous 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 <- "dichotomous"
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` *Plotting of Power Curve versus Correlate of Risk Effect Size for Continuous Biomarkers*

Description

Plots power (on the y-axis) to detect a correlate of risk effect size (on the x-axis) in the active treatment group for a continuous biomarker. The correlate of risk effect size is quantified as the relative risk ratio of the clinical endpoint per standard deviation increase for a noise-free biomarker.

Usage

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

Arguments

`outComputePower`	either a list or list of lists containing output from `computePower` or a character vector specifying the `.RData` file(s) containing `computePower` output
`outDir`	a character vector specifying path(s) to output `.RData` file(s), necessary if `outComputePower` is a character vector. Default is `NULL`.
`legendText`	a character vector specifying the entirety of the legend text. The order of the elements (i.e., 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 `plotVElatCont` by matching the CoR relative risk in the two plots and examining power compared to treatment (vaccine) efficacy. This sheds light on the importance of overall vaccine efficacy on power and allows correlates of risk results to be interpreted in terms of potential correlates of efficacy/protection.

Value

None. The function is called solely for plot generation.

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 *Plotting of Power versus Correlate of Risk Effect Size for Dichotomous and Trichotomous Biomarkers*

Description

Plots power (on the y-axis) to detect a correlate of risk effect size (on the x-axis) in the active treatment group for a dichotomous or trichotomous biomarker. The correlate of risk effect size is quantified as the relative risk ratio of the clinical endpoint comparing subgroups of active treatment recipients with high and low biomarker response.

Usage

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

Arguments

outComputePower	either a list or list of lists containing output from computePower or a character vector specifying the .RData file(s) containing computePower output
outDir	a character vector specifying path(s) to output .RData file(s), necessary if outComputePower is a character vector. Default is NULL.
legendText	a character vector specifying the entirety of the legend text. The order of the elements (i.e., 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 computePower, only the first level is used to determine the RR_t values that are plotted on the x-axis.

Value

None. The function is called solely for plot generation.

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)

# Set parameters for plotPowerTri function
# outComputePower is a list of lists containing outputs from the computePower function
outComputePower <- list(pwr1, pwr2)
legendText <- paste0("controls:cases = ", c("5:1","3:1"))
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")
outDir = rep("~/myDir", 2)
legendText <- paste0("controls:cases = ", c("5:1","3:1"))
plotPowerTri(outComputePower, outDir=outDir, legendText = legendText)

## End(Not run)
```

`plotROCcurveTri` *Plotting of ROC Curves for Trichotomous Biomarkers*

Description

Plots the receiver operating characteristic (ROC) curve displaying sensitivity and specificity for a range of `P2` and `P0` values, four values of `rho`, and four values of `Plat2`. Illustrates how different levels of measurement error `rho` map to sensitivity and specificity, depending on the value of `Plat2`. This funciton is used to create Figure 1 in the Supplementary Material of [Gilbert, Janes, and Huang (2016). "Power/Sample Size Calculations for Assessing Correlates of Risk in Clinical Efficacy Trials."]

Usage

```
plotROCcurveTri(Plat0, Plat2, P0, P2, rho)
```

Arguments

Plat0	a numeric value specifying the prevalence of the latent lower protected subgroup for a dichotomous or trichotomous biomarker
Plat2	a numeric vector of length four specifying the prevalences of the latent higher protected subgroup for a dichotomous or trichotomous biomarker
P0	a numeric vector specifying a grid of probabilities of low biomarker response for a dichotomous or trichotomous biomarker.
P2	a numeric vector specifying a grid of probabilities of high biomarker response for a dichotomous or trichotomous biomarker.
rho	a numeric vector of length four specifying distinct protection-relevant fractions of sigma2obs.

Value

None. The function is called solely for plot generation.

Examples

```
Plat0 <- 0.2
Plat2 <- c(0.2, 0.3, 0.4, 0.5)
P0 <- seq(0.90, 0.10, len=10)
P2 <- seq(0.10, 0.90, len=10)
rho <- c(1, 0.9, 0.7, 0.5)
plotROCcurveTri(Plat0 = Plat0, Plat2 = Plat2, P0 = P0, P2 = P2, rho = rho)
```

---

plotRRgradVE — *Plotting of the Ratio of Relative Risks for Higher/Lower Latent Subgroups against Correlate of Risk Effect Size for Trichotomous Biomarkers*

Description

Plots the ratio of relative risks for the higher and lower latent subgroups (on the y-axis) versus the correlate of risk effect size (on the x-axis) in the active treatment group for a trichotomous biomarker. The correlate of risk effect size is quantified as the relative risk ratio of the clinical endpoint comparing subgroups of active treatment recipients with high and low biomarker response.

Usage

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

Arguments

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

Details

When rho is varied, this plot shows how the relationship between the correlate of risk effect size and the relative risks for the higher and lower latent subgroups changes for different values of rho. The ratio of relative risks for the higher and lower latent subgroups is a relative vaccine efficacy parameter. When rho=1, a correlate of risk in the vaccine group is equivalent to the relative vaccine efficacy parameter, whereas for imperfectly measured biomarkers with rho<1, the correlate of risk effect size is closer to the null than the relative vaccine efficacy parameter is.

Value

None. The function is called solely for plot generation.

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` *Plotting Treatment (Vaccine) Efficacy Curves for Different Correlate of Risk Relative Risks for Continuous Biomarkers*

Description

Plots the treatment (vaccine) efficacy curve for the true latent biomarker for eight different values of the latent correlate of risk relative risk and the lowest vaccine efficacy level for the true biomarker. All curves assume `rho=1`, and treatment (vaccine) efficacy ranges from 0 to 1. The legend is completely determined by the function.

Usage

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

Arguments

`outComputePower`	a list containing output from `computePower` or a character string specifying the `.RData` file containing `computePower` output
`outDir`	a character string specifying path to output `.RData` file, necessary if `outComputePower` is a character string. Default is `NULL`.

Details

computePower function input parameter VElowest must have length greater than or equal to eight 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 corresponds to a flat curve where vaccine efficacy for all values of the true latent biomarker is equal to the overall vaccine efficacy. Increasing departures from the null hypothesis correspond to increasingly variable and steep VE curves. The output assumes the overall placebo-group endpoint risk between τ and τ_{max} is constant for all values of the latent and observed biomarker and that there is no measurement error ($\rho = 1$). When this is the case, an association of the biomarker with infection risk in the vaccine group (a correlate of risk) is equivalent to an association of the biomarker with treatment (vaccine) efficacy.

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

None. The function is called solely for plot generation.

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)
```

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