Package 'hctrial'

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Type Package

Title Using Historical Controls for Designing Phase II Clinical Trials

Version 0.1.0

Description Provides functions for designing phase II clinical trials adjusting for the heterogeneity of the population using known subgroups or historical controls.

Depends R (>= 3.5.0)

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Contents

`hctrial` *hctrial: A package for designing phase 2 clinical trials adjusting for heterogeneous populations.*

Description

The hctrial package provides functions for designing phase 2 clinical trials that adjust for the heterogeneity in the population.

Details

Two different ways are considered for designing a trial: based on known subgroups or based on historical data.

For initializing a stratified trial, use `strat_start`.

At interim, `strat_interim` should be used to adjust the trial.

At the end of the study, `strat_end` is used to adjust the trial again.

`hist_start`, `hist_interim` and `hist_end` work analogously, but are based on historical controls.

`hist_end` *Adjust a design based on historical controls at the end of the study using the covariate data of the patients accrued in stage 2.*

Description

Adjust a design based on historical controls at the end of the study using the covariate data of the patients accrued in stage 2.

Usage

```
hist_end(interim, stagetwo_data)
```

Arguments

`interim`	An design based on historical controls and adjusted at interim as returned by `hist_interim()`.
`stagetwo_data`	A dataframe containing the relevant covariate data of the patients accrued in stage 2.

Value

A list returning the arguments of the function and the final design of the trial.

Examples

```
X <- abs(rnorm(1000, 0, 1))
Y <- rbinom(1000, 1, 1-exp(-X))
mydata <- data.frame("X" = X, "Y" = Y)
start <- hist_start(mydata, Y~X, c1 = 2)
n1 <- start$des_start[2]
X1 <- abs(rnorm(n1, 0, 1))
dataone <- data.frame("X" = X1)
interim <- hist_interim(start, dataone)
n2 <- interim$des_interim[4]
X2 <- abs(rnorm(n2, 0, 1))
datatwo <- data.frame("X" = X2)
hist_end(interim, datatwo)
```

`hist_interim` *Adjust a design based on historical controls at interim using the covariate data of the patients accrued in stage 1.*

Description

Adjust a design based on historical controls at interim using the covariate data of the patients accrued in stage 1.

Usage

```
hist_interim(start, stageone_data)
```

Arguments

`start`	An initialized design based on historical controls as returned by `hist_start()`.
`stageone_data`	A dataframe containing the relevant covariate data of the patients accrued in stage 1.

Value

A list returning the arguments of the function and the preliminary design of a trial based on historical controls adjusted at interim.

Examples

```
X <- abs(rnorm(1000, 0, 1))
Y <- rbinom(1000, 1, 1-exp(-X))
mydata <- data.frame("X" = X, "Y" = Y)
start <- hist_start(mydata, Y~X, c1 = 2)
n1 <- start$des_start[2]
X1 <- abs(rnorm(n1, 0, 1))
dataone <- data.frame("X" = X1)
hist_interim(start, dataone)
```

`hist_start` *Initializes a design based on historical controls before the start of the study.*

Description

Initializes a design based on historical controls before the start of the study.

Usage

```
hist_start(hist_data, formula, phi = "odds_ratio", c1, modelfit = NULL,
  mean0 = NULL, mean1 = NULL, alpha = 0.05, beta = 0.2)
```

Arguments

`hist_data`	A data frame containing covariates and binary responses for historical controls.
`formula`	A formula which is used for fitting a logistic regression model on the historical data.
`phi`	The relation between the response rate under the null and the response rate under the interesting alternative. "odds_ratio" assumes that the odds ratio (OR) between these response rates is constant with OR = `c1+1`. "difference" assumes that the response rate under the alternative is `c1` higher than under the null. Can also be specified by the user by providing a function with arguments `c` and `x`.
`c1`	parameter for obtaining the response rate under the alternative, see description of phi.
`modelfit`	Can be used instead of `formula` and `hist_data` to provide an arbitrary fitted model that is compatible with `predict(modelfit, type="response")`. `formula` and `hist_data` are ignored if `modelfit` is specified.
`mean0`	Optional: Can be used to overwrite the estimated average response rate under the null of the fitted model.
`mean1`	Optional: Can be used to overwrite the estimated average response rate under the alternative of the fitted model.
`alpha`	Specified type I error of the trial.
`beta`	Specified type II error of the trial.

Value

A list returning the arguments of the function and the preliminary design for starting the stratified trial.

Examples

```
X <- abs(rnorm(1000, 0, 1))
Y <- rbinom(1000, 1, 1-exp(-X))
mydata <- data.frame("X" = X, "Y" = Y)
hist_start(mydata, Y~X, c1 = 2)
```

`strat_end` *Adjust a subspace stratified design at the end of the study.*

Description

Adjust a subspace stratified design at the end of the study.

Usage

```
strat_end(interim, sub_stagetwo)
```

Arguments

`interim`	A preliminary stratified design adjusted at interim as returned by `strat_interim()`.
`sub_stagetwo`	The subtypes observed for the patients accrued in stage 2.

Value

A list returning the arguments of the function and the final design of the stratified trial.

Examples

```
p0_sub <- c(0.1, 0.3, 0.5)
p1_sub <- c(0.3, 0.5, 0.7)
distr_sub <- c(1/3, 1/3, 1/3)
start <- strat_start(p0_sub, p1_sub, distr_sub)
n1 <- start$des_start[2]
subone <- sample(c(1,2,3), n1, TRUE)
interim <- strat_interim(start, subone)
n2 <- interim$des_interim[4]
subtwo <- sample(c(1,2,3), n2, TRUE)
strat_end(interim, subtwo)
```

`strat_interim` *Adjust a subspace stratified design at interim.*

Description

Adjust a subspace stratified design at interim.

Usage

```
strat_interim(start, sub_stageone)
```

Arguments

`start`	An initialized stratified design as returned by `strat_start()`.
`sub_stageone`	The subtypes observed for the patients accrued in stage 1.

Value

A list returning the arguments of the function and the preliminary design of a stratified trial adjusted at interim.

Examples

```
p0_sub <- c(0.1, 0.3, 0.5)
p1_sub <- c(0.3, 0.5, 0.7)
distr_sub <- c(1/3, 1/3, 1/3)
start <- strat_start(p0_sub, p1_sub, distr_sub)
n1 <- start$des_start[2]
subone <- sample(c(1,2,3), n1, TRUE)
strat_interim(start, subone)
```

`strat_start` *Initializes a subspace stratified design before the start of the study.*

Description

Initializes a subspace stratified design before the start of the study.

Usage

```
strat_start(p0_sub, p1_sub, distr_sub, alpha = 0.05, beta = 0.2)
```

Arguments

`p0_sub`	A vector, where the i-th entry corresponds to the response rate under the null for the i-th subtype.
`p1_sub`	A vector, where the i-th entry corresponds to the response rate under the alternative for the i-th subtype.
`distr_sub`	A vector, where the i-th entry corresponds to the prevalence of the i-th subtype in the population.
`alpha`	Specified type I error of the trial.
`beta`	Specified type II error of the trial.

Value

A list returning the arguments of the function and the preliminary design for starting the stratified trial.

Examples

```
p0_sub <- c(0.1, 0.3, 0.5)
p1_sub <- c(0.3, 0.5, 0.7)
distr_sub <- c(1/3, 1/3, 1/3)
strat_start(p0_sub, p1_sub, distr_sub)
```

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