Package 'ewhorm'

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Title Statistical Considerations for Designing e-WHORM Adaptive Trial

Version 0.1

Author Marta Bofill Roig [aut, cre] (<https://orcid.org/0000-0002-4400-7541>), Martin Posch [aut], Sonja Zehetmayer [aut]

Maintainer Marta Bofill Roig <marta.bofillroig@meduniwien.ac.at>

Description Data simulation and analysis for the design of e-WHORM trial

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Encoding UTF-8

Imports mvtnorm,
stats,
multcomp,
gMCP,
gtools

Roxygen list(markdown = TRUE)

RoxygenNote 7.2.1

Suggests knitr,
rmarkdown

VignetteBuilder knitr

R topics documented:

get_hyp_mat *Function to compute the hypotheses to test (closed test)*

Description

Function to compute the hypotheses to test (closed test)

Usage

```
get_hyp_mat(n_hypothesis = 3, selected_hypothesis = 1)
```

Arguments

n_hypothesis	num elementary hypotheses
selected_hypothesis	selected hypothesis for closed test

Details

eWHORM simulations

Value

maximum value in a row

Author(s)

Marta Bofill Roig

get_max_col_index *Function to get the column index of the maximum value in a row*

Description

Function to get the column index of the maximum value in a row

Usage

```
get_max_col_index(row)
```

Arguments

row	selected row

Details

eWHORM simulations

Value

maximum value in a row

Author(s)

Marta Bofill Roig

`sim_data` *Simulate data from a multi-arm trial with shared control*

Description

Function to simulate trial data (1-stage, multiple arms)

Usage

```
sim_data(n_arms, N, mu_6m, mu_12m, sigma, rmonth)
```

Arguments

`n_arms`	number of arms (including control)
`N`	total sample size
`mu_6m`	6-month mean response per arm (vector of length `n_arm`)
`mu_12m`	12-month mean response per arm (vector of length `n_arm`)
`sigma`	covariance matrix between 6- and 12-month responses assumed equal across arms (matrix of dim 2x2)
`rmonth`	recruitment per month (recruitment speed assumed constant over time)

Details

eWHORM simulations

Value

simulated data consisting of the responses at 6 and 12 months, treatment arm, and recruitment time for each subject.

Author(s)

Marta Bofill Roig

`sim_trial` *Simulate data from a multi-arm multi-stage trial with shared control and dose selection*

Description

Function to simulate trial data (2-stages, with dose selection). Analysis using Dunnett test in stage 1 and closed test for the selected dose, and the Inverse normal combination test for combining pvalues of stages 1 and 2.

Usage

```
sim_trial(
  n_arms = 4,
  N1 = 30 * 4,
  N2 = 30 * 2,
  mu_6m,
  mu_12m,
  sigma,
  rmonth,
  alpha1 = 0.5,
  alpha = 0.05,
  p_safety = c(0.9, 0.8, 0.7),
  safety = T,
  promising = F
)
```

Arguments

`n_arms`	number of arms (including control)
`N1`	sample size stage 1
`N2`	sample size stage 2
`mu_6m`	6-month mean response per arm (vector of length `n_arm`)
`mu_12m`	12-month mean response per arm (vector of length `n_arm`)
`sigma`	covariance matrix between 6- and 12-month responses assumed equal across arms (matrix of dim 2x2)
`rmonth`	recruitment per month (recruitment speed assumed constant over time)
`alpha1`	significance level for dose selection
`alpha`	significance level for selected dose vs control comparison
`p_safety`	probability of each dose to be safe
`safety`	indicator - if true, it simulates safety according to `p_safety`
`promising`	select the most promising dose at the interim analysis

Details

eWHORM simulations

Value

Combined p-value, selected dose and safety for each dose (if argument `safety=TRUE`)

Author(s)

Marta Bofill Roig

`sim_trial_pce` *Simulate data from a multi-arm multi-stage trial with shared control and two initial doses, where an additional dose could be added after the interim analysis*

Description

Function to simulate trial data (2-stages, with dose selection). The analyses are performed using partial conditional error.

Usage

```
sim_trial_pce(
  n_arms = 4,
  N1 = 30 * 4,
  N2 = 30 * 2,
  mu_6m,
  mu_12m,
  sigma,
  rmonth,
  alpha1 = 0.1,
  alpha = 0.05,
  v = c(1/2, 1/2, 0),
  sim_out = F
)
```

Arguments

`n_arms`	number of arms (including control)
`N1`	sample size stage 1
`N2`	sample size stage 2
`mu_6m`	6-month mean response per arm (vector of length `n_arm`)
`mu_12m`	12-month mean response per arm (vector of length `n_arm`)
`sigma`	covariance matrix between 6- and 12-month responses assumed equal across arms (matrix of dim 2x2)
`rmonth`	recruitment per month (recruitment speed assumed constant over time)
`alpha1`	significance level for dose selection
`alpha`	significance level for selected dose vs control comparison
`v`	vector giving the proportions of pre-planned measurements collected up to the interim analysis
`sim_out`	Option for simplified output for simulations (if `sim_out=TRUE` simplified version, the value is `FALSE` by default)

Details

eWHORM simulations

Value

A list consisting of pvalues at stage 1, pvalues at stage 2, the decision at stages 1 and 2, the selected dose at stage 1, and the time at which the last patient was recruited in stage 1 and 2.

Author(s)

Marta Bofill Roig

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