Package 'adpss'

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Title Design and Analysis of Locally or Globally Efficient Adaptive Designs

Version 0.1.1

Description Provides the functions for planning and conducting a clinical trial with adaptive sample size determination. Maximal statistical efficiency will be exploited even when dramatic or multiple adaptations are made. Such a trial consists of adaptive determination of sample size at an interim analysis and implementation of frequentist statistical test at the interim and final analysis with a prefixed significance level. The required assumptions for the stage-wise test statistics are independent and stationary increments and normality. Predetermination of adaptation rule is not required.

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License GPL (>= 2)

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URL https://github.com/ca4wa/R-adpss

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`adpss-package` *adpss: A package for design and analysis of a locally or globally efficient adaptive design involving adaptive sample size determination.*

Description

This package provides the functions for conducting a trial with adaptive sample size determination. Such a trial consists of adaptive determination of sample size at an interim analysis and implementation of frequentist statistical test of a prefixed significance level. The required assumptions for the stochastic process of the test statistics is Brownian motion. Predetermination of adaptation rule is not required, i.e., adaptations can be made with full flexibility.

`adaptive_analysis_norm_global` *Analyze data according to a globally efficient adaptive design.*

Description

`adaptive_analysis_norm_global` performs an globally efficient adaptive test, a Frequentist adaptive test with the specified significance level with full flexibility. Normality with known variance is assumed for the test statistic (more accurately, the test statistic is assumed to follow Brownian motion.) Null hypothesis is fixed at 0 without loss of generality. Exact p-value, median unbiased estimate and confidence limits proposed by Gao et al. (2013) can also be calculated. For detailed illustration, see `vignette("adpss_ex")`.

Usage

```
adaptive_analysis_norm_global(initial_test = 0, times = 0, stats = 0,
  costs = 0, final_analysis = TRUE, estimate = TRUE, ci_coef = 0.95,
  tol_est = 1e-08, input_check = TRUE)
```

Arguments

initial_test	Designate the initial working test generated by work_test_norm_global function.
times	The sequence of times (sample size or information level) at which analyses were conducted.
stats	The sequence of test statistics.
costs	The sequence of loss required to construct working tests. Specification is optional. Partial specification is allowed, in which non-specification may be represented by 0.
final_analysis	If TRUE, the result input will be regarded as complete (no more data will be obtained) and the significance level will be exhausted. If FALSE, the current analysis will be regarded as an interim analysis and the significance level will be preserved.
estimate	If TRUE, p-value, median unbiased estimator and upper and lower confidence limits will be calculated.
ci_coef	The confidence coefficient. Default is 0.95.
tol_est	The precision of the calculated results.
input_check	Indicate whether or not the arguments input by user contain invalid values.

Value

It returns whether or not the result was statistically significant, a p-value and an exact confidence limits.

References

Kashiwabara, K., Matsuyama, Y. An efficient adaptive design approximating fixed sample size designs. In preparation. Gao, P., Liu, L., Mehta, C. (2013) Exact inference for adaptive group sequential designs. Stat Med 32: 3991-4005.

See Also

work_test_norm_global and sample_size_norm_global.

Examples

```
# Construct an initial working test
# Note: cost_type_1_err will be automatically calculated when 0 is specified.
init_work_test <- work_test_norm_global(min_effect_size = -log(0.65), cost_type_1_err=1683.458)

# Sample size calculation
sample_size_norm_global(
  initial_test = init_work_test,
  effect_size = 11.11 / 20.02, # needs not be MLE
  time = 20.02,
  target_power = 0.75,
  sample_size = TRUE
  )
```

adaptive_analysis_norm_local *Analyze data according to a locally efficient adaptive design.*

Description

adaptive_analysis_norm_local performs an locally efficient adaptive test, a Frequentist adaptive test with the specified significance level with full flexibility. Normality with known variance is assumed for the test statistic (more accurately, the test statistic is assumed to follow Brownian motion.) Null hypothesis is fixed at 0 without loss of generality. No procedure to calculate p-value or confidence intervals is employed. For detailed illustration, see `vignette("adpss_ex")`.

Usage

```
adaptive_analysis_norm_local(overall_sig_level = 0.025, min_effect_size = 1,
  times = 0, stats = 0, final_analysis = TRUE, estimate = FALSE,
  ci_coef = 0.95, input_check = TRUE)
```

Arguments

overall_sig_level	Overall significance level in (0, 1). Default is 0.025.
min_effect_size	The minimum effect size. It should be positive. The working test will be constructed to have the power of `1 - work_beta` for this effect size. Default is 1.
times	The sequence of times (sample size or information level) at which analyses were conducted.
stats	The sequence of test statistics.
final_analysis	If TRUE, the result input will be regarded as complete (no more data will be obtained) and the significance level will be exhausted. If FALSE, the current analysis will be regarded as an interim analysis and the significance level will be preserved.
estimate	If TRUE, p-value, median unbiased estimator and upper and lower confidence limits will be calculated.
ci_coef	The confidence coefficient. Default is 0.95.
input_check	Indicate whether or not the arguments input by user contain invalid values.

Value

List of results including the conditional Type I error probability.

References

Kashiwabara, K., Matsuyama, Y. An efficient adaptive design approximating fixed sample size designs. In preparation.

See Also

sample_size_norm_local.

Examples

```
# Sample size calculation
sample_size_norm_local(
  overall_sig_level = 0.025,
  min_effect_size = -log(0.65),
  effect_size = 11.11 / 20.02, # needs not be MLE
  time = 20.02,
  target_power = 0.75,
  sample_size = TRUE
  )
```

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sample_size_norm_global

Calculate sample size or power for a globally efficient adaptive design.

Description

sample_size_norm_global calculates the power if the time of the final analysis is given and otherwise the sample size. The computed power for effect_size is an approximate lower bound. Sample size is also calculated on the basis of the bound.

Usage

```
sample_size_norm_global(initial_test = 0, sample_size = TRUE,
  effect_size = 0, time = 0, target_power = 0.8, final_time = 0,
  tol_sample_size = 1e-05, input_check = TRUE)
```

Arguments

initial_test	Designate the initial working test generated by work_test_norm_global function.
sample_size	If TRUE, the function will return the sample size required by the globally efficient adaptive design to have the power of target_power. If FALSE, the function will return the power when the final interim analysis and the final analysis are conducted at time and final_time, respectively.
effect_size	The effect size, on the basis of which the power or sample size calculation will be performed. In globally efficient designs, any real value is allowed.
time	The time of the current analysis.
target_power	The power, on the basis of which the sample size calculation will be performed.
final_time	The time of the final analysis.
tol_sample_size	The precision in calculation of the sample size.
input_check	Indicate whether or not the arguments input by user contain invalid values.

Value

It returns the sample size (when `sample_size = TRUE`) or the power (when `sample_size = FALSE`).

See Also

`adaptive_analysis_norm_global` for example of this function.

`sample_size_norm_local` *Calculate sample size or power for a locally efficient adaptive design.*

Description

`sample_size_norm_local` calculates the power if the time of the final analysis is given and otherwise the sample size. The computed power for `effect_size` is an approximate lower bound. Sample size is also calculated on the basis of the bound.

Usage

```
sample_size_norm_local(overall_sig_level = 0.025, min_effect_size = 1,
  sample_size = TRUE, effect_size = 1, time = 0, target_power = 0.8,
  final_time = 0, tol_sample_size = 1e-08, input_check = TRUE)
```

Arguments

`overall_sig_level`	Overall significance level in (0, 1). Default is 0.025.
`min_effect_size`	The minimum effect size. It should be positive. The working test will be constructed to have the power of `1 - work_beta` for this effect size. Default is 1.
`sample_size`	If `TRUE`, the function will return the sample size required by the locally efficient adaptive design to have the power of `target_power`. If `FALSE`, the function will return the power when the final interim analysis and the final analysis are conducted at `time` and `final_time`, respectively.
`effect_size`	The effect size, on the basis of which the power or sample size calculation will be performed. In locally efficient adaptive designs, any real value no less than `min_effect_size / 2` is allowed.
`time`	The time of the current analysis.
`target_power`	The power, on the basis of which the sample size calculation will be performed.
`final_time`	The time of the final analysis.
`tol_sample_size`	The precision in calculation of the sample size.
`input_check`	Indicate whether or not the arguments input by user contain invalid values.

Value

It returns the sample size (when `sample_size = TRUE`) or the power (when `sample_size = FALSE`).

See Also

`adaptive_analysis_norm_local` for example of this function.

`work_test_norm_global` *Construct a working test and implement an interim or the final analysis for a globally efficient adaptive design.*

Description

This function is used as a routine by `adaptive_analysis_norm_global` and `sample_size_norm_global`.

Usage

```
work_test_norm_global(overall_sig_level = 0.025, work_beta = 0.05,
  cond_alpha = overall_sig_level, cost_type_1_err = 0,
  cost_type_2_err = 0, prev_cost = 0, min_effect_size = 1,
  effect_size = 0, basic_schedule_num = 50, basic_schedule_power = 2,
  basic_schedule = 0, prior_dist = 0, prev_time = 0, time = 0,
  next_time = 0, stat = 0, input_check = TRUE, out_process = FALSE,
  simpson_div = 6, tol_boundary = 1e-08, tol_cost = 1e-08)
```

Arguments

`overall_sig_level`
: Overall significance level in (0, 1). Default is 0.025.

`work_beta`
: Type II error probability of the working test. Default is 0.05.

`cond_alpha`
: Conditional Type I error probability in (0, 1). Default is 0.025.

`cost_type_1_err`
: The loss caused by erroneously rejecting the null hypothesis. If 0 is specified, the loss leading to the working test with its Type I error probability being `significance_level` will be calculated. Default is 0.

`cost_type_2_err`
: The loss caused by erroneously accepting the null hypothesis. If 0 is specified, the loss will be set to the value of the maximum of the basic analysis schedule. Default is 0.

`prev_cost`
: The value of `cost_type_1_err` of the working test in the analysis just before the current analysis.

`min_effect_size`
: The minimum effect size. It should be positive. The working test will be constructed to have the power of `1 - work_beta` for this effect size. Default is 1.

`effect_size` The effect size for which the probability of rejecting the null hypothesis will be calculated. If `cost_type_1_err = 0`, `effect_size` will be forced to be the null value, 0. Default is 0.

`basic_schedule_num`
The number of analysis of the working test. Default is 50.

`basic_schedule_power`
Determine the intervals between analyses. Default is 2.

`basic_schedule` The basic analysis schedule arbitrarily specified by user.

`prior_dist` Prior distribution for effect sizes of `min_effect_size * 0:10 / 2`.

`prev_time` The time of the analysis just before the current analysis. Either `prev_time` or `next_time` should be 0. See the example below.

`time` The time of the current analysis.

`next_time` The time of the next analysis. Either `prev_time` or `next_time` should be 0. See the example below.

`stat` The value of the current test statistic. The value of `stat` should be 0 at `time = 0`.

`input_check` Indicate whether or not the arguments input by user contain invalid values.

`out_process` The values used in calculation will be output in addition to the main output. Default is FALSE.

`simpson_div` The precision determining the precision of numerical integration. The default value is 6.

`tol_boundary` The precision in calculation of the stopping boundary of the working test.

`tol_cost` The precision in calculation of the loss, `cost_type_1_error`.

Value

List of values of the parameters specified, information of the working test, and the conditional probability of rejecting the null hypothesis.

See Also

`adaptive_analysis_norm_global` for example of this function.

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