Package 'ASSISTant'

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Type Package

Title Adaptive Subgroup Selection in Group Sequential Trials

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VignetteBuilder knitr

URL https://github.com/bnaras/ASSISTant

BugReports https://github.com/bnaras/ASSISTant/issues

Description Clinical trial design for subgroup selection in three-stage group sequential trial. Includes facilities for design, exploration and analysis of such trials. An implementation of the initial DEFUSE-3 trial is also provided as a vignette.

License GPL (>= 2)

RoxygenNote 5.0.1

Imports R6, mvtnorm

Suggests knitr, rmarkdown

NeedsCompilation no

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R topics documented:

`ASSISTant` *Three stage group sequential adaptive design with subgroup selection*

Description

`ASSISTant` is a package that implements a three-stage adaptive clinical trial design with provision for subgroup selection where the treatment may be effective. The main design object is an `R6` class that can be instantiated and manipulated to obtain the operating characteristics. A vignette is provided showing the use of this package for designing the DEFUSE-3 trial, described in the paper by Lai, Lavori and Liao. The package contains everything necessary to reproduce the results of the paper.

References

Adaptive Choice of Patient Subgroup for Comparing Two Treatments by Tze Leung Lai and Philip W. Lavori and Olivia Yueh-Wen Liao. Contemporary Clinical Trials, Vol. 39, No. 2, pp 191-200 (2014). http://www.sciencedirect.com/science/article/pii/S1551714414001311

Adaptive design of confirmatory trials: Advances and challenges, http://www.sciencedirect.com/science/article/pii/S1551714415300239 by Tze Leung Lai and Philip W. Lavori and Ka Wai Tsang. Contemporary Clinical Trials, Vol. 45, Part A, pp 93-102 (2015).

`ASSISTDesign` *A class to encapsulate the adaptive clinical trial design of Lai, Lavori and Liao*

Description

`ASSISTDesign` objects are used to design, simulate and analyze adaptive group sequential clinical trial with three stages.

Usage

```
ASSISTDesign
```

Format

An `R6Class` generator object

Methods

`ASSISTDesign$new(designParameters, trialParameters, generateData)` Create a new `ASSISTDesign` instance object using the parameters specified

`getDesignParameters`,`getTrialParameters`, `getBoundaries` Accessor methods for (obvious) object fields

`print()` Print the object in a human readable form

`computeCriticalValues()` Compute the critical boundary values $\tilde{b}$, b and c for futility, efficacy and final efficacy decisions; saved in field `boundaries`

`explore(numberOfSimulations = 5000, rngSeed = 12345, effectiveParameters = self$getDesignParameters` Explore the design using the specified number of simulations and random number seed. `trueParameters` is by default the same as `designParameters` as would be the case for a Type I error calculation. If changed, would yield power. Show progress if so desired. Returns a data frame of results

`analyze(trialHistory)` Analyze the design given the `trialHistory` which is the result of a call to `explore` to simulate the design. Return a list of summary quantities

`summary(analysis)` Print the operating characteristics of the design, using the analysis result from the `analyze` call

References

Adaptive Choice of Patient Subgroup for Comparing Two Treatments by Tze Leung Lai and Philip W. Lavori and Olivia Yueh-Wen Liao. Contemporary Clinical Trials, Vol. 39, No. 2, pp 191-200 (2014). http://www.sciencedirect.com/science/article/pii/S1551714414001311

See Also

`LLL.SETTINGS` for an explanation of trial parameters

Examples

```
## Not run:
data(LLL.SETTINGS)
prevalence <- LLL.SETTINGS$prevalences$table1
scenario <- LLL.SETTINGS$scenarios$S0
designParameters <- list(prevalence = prevalence,
                      mean = scenario$mean,
                      sd = scenario$sd)
designA <- ASSISTDesign$new(trialParameters = LLL.SETTINGS$trialParameters,
                            designParameters = designParameters)
print(designA)
## A realistic design uses 5000 simulations or more!
result <- designA$explore(showProgress = interactive())
analysis <- designA$analyze(result)
designA$summary(analysis)

## End(Not run)
## For full examples, try:
## browseURL(system.file("full_doc/ASSISTant.html", package="ASSISTant"))
```

ASSISTDesignB *A fixed sample design to compare against the adaptive clinical trial design of Lai, Lavori and Liao.*

Description

ASSISTDesignB objects are used to design a trial with certain characteristics provided in the object instantiation method. This design differs from ASSISTDesign in only how it computes the critical boundaries, how it performs the interim look, and what quantities are computed in a trial run.

Usage

```
ASSISTDesignB
```

Format

An R6Class generator object

Methods

`ASSISTDesignB$new(designParameters, trialParameters, generateData)` Create a new ASSISTDesign instance object using the parameters specified.

`getDesignParameters`,`getTrialParameters`, `getBoundaries` Accessor methods for (obvious) object slots

`print()` Print the object in a human readable form

`computeCriticalValues()` Compute the critical boundary value c_α

`explore(numberOfSimulations = 5000, rngSeed = 12345, trueParameters = self$getDesignParameters(), s` Explore the design using the specified number of simulations and random number seed. `trueParameters` is by default the same as `designParameters` as would be the case for a Type I error calculation. If changed, would yield power. Show progress if so desired. Returns a data frame of results

`analyze(trialHistory)` Analyze the design given the `trialHistory` which is the result of a call to `explore` to simulate the design. Return a list of summary quantities

`summary(analysis)` Print the operating characteristics of the design, using the analysis result from the `analyze` call

References

Adaptive Choice of Patient Subgroup for Comparing Two Treatments by Tze Leung Lai and Philip W. Lavori and Olivia Yueh-Wen Liao. Contemporary Clinical Trials, Vol. 39, No. 2, pp 191-200 (2014). http://www.sciencedirect.com/science/article/pii/S1551714414001311

See Also

ASSISTDesign which is a superclass of this object

Examples

```
## Not run:
data(LLL.SETTINGS)
prevalence <- LLL.SETTINGS$prevalences$table1
scenario <- LLL.SETTINGS$scenarios$S0
designParameters <- list(prevalence = prevalence,
                         mean = scenario$mean,
                         sd = scenario$sd)
designB <- ASSISTDesignB$new(trialParameters = LLL.SETTINGS$trialParameters,
                             designParameters = designParameters)
print(designB)
## A realistic design uses 5000 simulations or more!
result <- designB$explore(showProgress = interactive())
analysis <- designB$analyze(result)
designB$summary(analysis)

## End(Not run)
## For full examples, try:
## browseURL(system.file("full_doc/ASSISTant.html", package="ASSISTant"))
```

`ASSISTDesignC` *A fixed sample RCT design to compare against the adaptive clinical trial design of Lai, Lavori and Liao.*

Description

`ASSISTDesignC` objects are used to design a trial with certain characteristics provided in the object instantiation method. This design differs from `ASSISTDesign` in only how it computes the critical boundaries, how it performs the interim look, and what quantities are computed in a trial run.

Usage

```
ASSISTDesignC
```

Format

An `R6Class` generator object

Methods

`ASSISTDesignC$new(designParameters, trialParameters, generateData)` Create a new `ASSISTDesign` instance object using the parameters specified.

`getDesignameters`,`getTrialParameters`, `getBoundaries` Accessor methods for (obvious) object slots

`print()` Print the object in a human readable form

`computeCriticalValues()` Compute the critical boundary value c_α

`explore(numberOfSimulations = 5000, rngSeed = 12345, trueParameters = self$getDesignParameters(), s`
Explore the design using the specified number of simulations and random number seed. `trueParameters` is by default the same as `designParameters` as would be the case for a Type I error calculation. If changed, would yield power. Show progress if so desired. Returns a data frame of results

`analyze(trialHistory)` Analyze the design given the `trialHistory` which is the result of a call to `explore` to simulate the design. Return a list of summary quantities

`summary(analysis)` Print the operating characteristics of the design, using the analysis result from the `analyze` call

References

Adaptive Choice of Patient Subgroup for Comparing Two Treatments by Tze Leung Lai and Philip W. Lavori and Olivia Yueh-Wen Liao. Contemporary Clinical Trials, Vol. 39, No. 2, pp 191-200 (2014). http://www.sciencedirect.com/science/article/pii/S1551714414001311

See Also

`ASSISTDesignB` which is a superclass of this object

Examples

```
data(LLL.SETTINGS)
prevalence <- LLL.SETTINGS$prevalences$table1
scenario <- LLL.SETTINGS$scenarios$S0
designParameters <- list(prevalence = prevalence,
                         mean = scenario$mean,
                         sd = scenario$sd)
## A realistic design uses 5000 simulations or more!
designC <- ASSISTDesignC$new(trialParameters = LLL.SETTINGS$trialParameters,
                             designParameters = designParameters)
print(designC)
result <- designC$explore(numberOfSimulations = 100, showProgress = interactive())
analysis <- designC$analyze(result)
designC$summary(analysis)
## For full examples, try:
## browseURL(system.file("full_doc/ASSISTant.html", package="ASSISTant"))
```

DEFUSE3Design *The DEFUSE3 design*

Description

`DEFUSE3Design` is a slight variant of the the adaptive clinical trial design of Lai, Lavori and Liao. Simulation is used to compute the expected maximum sample size and the boundary for early futility is adjusted to account as well.

Usage

```
DEFUSE3Design
```

Format

An R6Class generator object

Methods

`DEFUSE3Design$new(designParameters, trialParameters, generateData, numberOfSimulations = 5000, rngS` Create a new ASSISTDesign instance object using the parameters specified.

`getDesignParameters`,`getTrialParameters`, `getBoundaries` Accessor methods for (obvious) object slots

`print()` Print the object in a human readable form

`adjustCriticalValues(numberOfSimulations, rngSeed, showProgress)` Adjust the critical values by performing simulations using the parameters provided

`computeCriticalValues()` Compute the critical boundary value c_α

`explore(numberOfSimulations = 5000, rngSeed = 12345, trueParameters = self$getDesignParameters(). s` Explore the design using the specified number of simulations and random number seed. `trueParameters` is by default the same as `designParameters` as would be the case for a Type I error calculation. If changed, would yield power. Show progress if so desired. Returns a data frame of results

`analyze(trialHistory)` Analyze the design given the `trialHistory` which is the result of a call to `explore` to simulate the design. Return a list of summary quantities

`summary(analysis)` Print the operating characteristics of the design, using the analysis result from the `analyze` call

References

Adaptive design of confirmatory trials: Advances and challenges, http://www.sciencedirect.com/science/article/pii/S1551714415300239 by Tze Leung Lai and Philip W. Lavori and Ka Wai Tsang. Contemporary Clinical Trials, Vol. 45, Part A, pp 93-102 (2015).

See Also

`ASSISTDesign` which is a superclass of this object

Examples

```
trialParameters <- list(N = c(200, 340, 476), type1Error = 0.025,
                        eps = 1/2, type2Error = 0.1)
designParameters <- list(
   nul0 = list(prevalence = rep(1/6, 6), mean = matrix(0, 2, 6),
               sd = matrix(1, 2, 6)),
   alt1 = list(prevalence = rep(1/6, 6), mean = rbind(rep(0, 6),
               c(0.5, 0.4, 0.3, 0, 0, 0)),
               sd = matrix(1, 2, 6)),
   alt2 = list(prevalence = rep(1/6, 6), mean = rbind(rep(0, 6),
```

```
              c(0.5, 0.5, 0, 0, 0, 0)),
              sd = matrix(1,2, 6)),
   alt3 = list(prevalence = rep(1/6, 6), mean = rbind(rep(0, 6), rep(0.36, 6)),
              sd = matrix(1,2, 6)),
   alt4 = list(prevalence = rep(1/6, 6), mean = rbind(rep(0, 6), rep(0.30, 6)),
              sd = matrix(1,2, 6)),
   alt5 = list(prevalence = rep(1/6, 6), mean = rbind(rep(0, 6),
              c(0.4, 0.3, 0.2, 0, 0, 0)),
              sd = matrix(1,2, 6)),
   alt6 = list(prevalence = rep(1/6, 6), mean = rbind(rep(0, 6),
              c(0.5, 0.5, 0.3, 0.3, 0.1, 0.1)),
              sd = matrix(1,2, 6)))

## Not run:
## A realistic design uses 5000 simulations or more!
defuse3 <- DEFUSE3Design$new(trialParameters = trialParameters,
                             numberOfSimulations = 25,
                             designParameters = designParameters$nul0,
                             showProgress = FALSE)
print(defuse3)
result <- defuse3$explore(showProgress = interactive())
analysis <- defuse3$analyze(result)
print(defuse3$summary(analysis))

## End(Not run)
## For full examples, try:
## browseURL(system.file("full_doc/defuse3.html", package="ASSISTant"))
```

`LLL.SETTINGS` *Design and trial settings used in the Lai, Lavori, Liao paper simulations*

Description

A list of design and trial design settings used for analysis and simulations in the Lai, Lavori, Liao paper displayed in Tables 1 and 2. The elements of the list are the following

trialParameters **N** the sample size at each of three interim looks, the last being the final one; The length of this also determines the number of interim looks

type1Error the overall type I error

eps the fraction of type I error spent at each interim look

type2Error the type II error desired

scenarios A list of the 10 settings used in the simulations named `S0`, `S1`, ..., `S10` as in the paper, each with three elements

mean a $2 \times J$ matrix of means, the first row for the null setting, the second for the alternative

sd a $2 \times J$ matrix of standard deviations, the first row for the null setting, the second for the alternative

prevalences A list of two elements with prevalence vectors used in the paper; the lengths of these vectors implicitly define the number of groups.

table1 a vector of equal prevalences for six groups used in table 1

table2 a vector of prevalences used in table 2 of the paper

References

Adaptive Choice of Patient Subgroup for Comparing Two Treatments by Tze Leung Lai and Philip W. Lavori and Olivia Yueh-Wen Liao. Contemporary Clinical Trials, Vol. 39, No. 2, pp 191-200 (2014). http://www.sciencedirect.com/science/article/pii/S1551714414001311

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