Package 'WRMT'

May 6, 2025

Title Win Ratio with Multiple Thresholds for Composite Endpoints

Version 0.1.0

Description This package provides the WRMT (win ratio with multiple thresholds) and WRAT (win ratio with adaptive thresholds) analyses for composite endpoints in clinical trials, based on the methodology in Mou et al. (2024, arXiv:2407.18341).

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Imports dplyr

Depends R (>= 3.5)

LazyData true

Contents

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adaptive.threshold.calipers

Obtain adaptive thresholds with caliper c specified for each outcome

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Description

This function calculates adaptive thresholds for WRAT analysis with caliper c specified for each outcome. To be called by function `WRAT()`.

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Usage

```
adaptive.threshold.calipers(
  pair.data,
  num.outcome,
  calipers,
  clinical.threshold = NULL
)
```

Arguments

pair.data   A data frame for pairwise comparison, returned by `data.to.pair()`.

num.outcome   A numeric value of the number of outcomes.

clinical.threshold

        A numeric vector represents the minimal clinical thresholds. Default to 0 for all endpoints.

caliper   A numeric vector indicates the caliper c used for each outcome.

Value

A list of outputs:

threshold A numeric vector of obtained adaptive thresholds.

stage A numeric vector indicating outcome for each comparison stage.

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adaptive.threshold.weights

> *Obtain adaptive thresholds with universal caliper c and weights w #'*
> *@description This function calculates adaptive thresholds for WRAT*
> *analysis with universal caliper c and weights w. To be called by func-*
> *tion* `WRAT()`.

Description

Obtain adaptive thresholds with universal caliper c and weights w #' @description This function calculates adaptive thresholds for WRAT analysis with universal caliper c and weights w. To be called by function `WRAT()`.

Usage

```
adaptive.threshold.weights(
  pair.data,
  num.outcome,
  weight,
  caliper = 0.2,
  clinical.threshold = NULL
)
```

Arguments

pair.data   A data frame for pairwise comparison, returned by `data.to.pair()`.

num.outcome   A numeric value of the number of outcomes.

weight   A numeric vector indicates the weights w for adaptive thresholds.

caliper   A numeric value indicates the universal caliper c for adaptive thresholds.

clinical.threshold
           A numeric vector represents the minimal clinical thresholds. Default to 0 for all endpoints.

Value

A list of outputs:

threshold A numeric vector of obtained adaptive thresholds.

stage A numeric vector indicating outcome for each comparison stage.

---

comparison.result   *Summarize comparison results for outputs*

Description

This function analyzes pairwise comparisons results provided by `WRMT.comparison()` or `WRAT.comparison()`. To be called by function `WRMT()` or `WRAT()`.

Usage

```
comparison.result(comparison.output)
```

Arguments

comparison.output
           A list returned by `WRMT.comparison()` or `WRAT.comparison()`. Must contain elements `pair.data`, `stage.results`, `treatment`, and `strata`.

Value

A list of analysis results:

WR A numeric value. Estimated win ratio for treatment versus control.

P A numeric value. Two-sided P value of the Finkelstein-Schoenfeld (FS) test.

Stage.decompose A list of stage-level comparison results for each stratum. Each stratum corresponds to a matrix. A single matrix will be returned for non-stratified analysis for simplicity. The decomposition matrix presents proportions of wins, ties, and losses (obtained by the treatment group) at each stage. Proportions are always obtained with respect to the total number of comparisons between treatment and control groups.

strata.summary A data frame presents strata weights and stratum-specific WR results.

FS.stat A numeric value of the FS test statistic.

FS.stat.var A numeric value of the variance of the FS test statistic.

Examples

```
# Example 1: stratified comparison
strata.compare <- WRMT.comparison(data = sample_data[,1:6],
                                  threshold = c(0,0), stage = c(1,2),
                                  direction = c(1,1),
                                  strata = sample_data$strata,
                                  strata.weight = NULL)
analysis.result <- comparison.result(strata.compare)
cat("WR:",analysis.result$WR, "; P-value:", analysis.result$P,"\n")

# Example 2: non-stratified comparison
nonstrata.compare <- WRMT.comparison(data = sample_data[,1:6],
                                     threshold = c(0,0), stage = c(1,2),
                                     direction = c(1,1),
                                     strata = NULL,
                                     strata.weight = NULL)
analysis.result <- comparison.result(nonstrata.compare)
cat("WR:",analysis.result$WR, "; P-value:", analysis.result$P,"\n")
```

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data.to.pair   *Organize dataset for pairwise comparison*

Description

Organize dataset for pairwise comparison

Usage

```
data.to.pair(data)
```

Arguments

data   Input data frame

Value

A data frame for pairwise comparison

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sample_data   *Sample dataset for WRMT analysis*

Description

A simulated dataset for demonstration purposes. This dataset has to time-to-event endpoints with poential administrative right censoring (i.e., maximal follow-up time set to 1000 time units), where the second event may be censored by the first event (i.e., semi-competing risk). The columns include:

- ID: Numeric participant ID.
- treat: 1 = Treatment group, 0 = Control group.

- `T1`: Observed value of the frist time-to-event endpoint.
- `C1`: Censoring indicator for T1 (1 = Censored, 0 = Event observed).
- `T2`: Observed value of the second time-to-event endpoint.
- `C2`: Censoring indicator for T2.
- `strata`: Strata information (with 3 different strata).

Usage

```
sample_data
```

Format

A data frame with 2000 rows and 7 columns.

Examples

```
data(sample_data)
head(sample_data)
```

WRAT *WRAT Analysis*

Description

Perform WRAT (win ratio with adaptive thresholds) analysis.

Usage

```
WRAT(
  data,
  method = c("weights", "calipers"),
  weights = NULL,
  calipers = NULL,
  clinical.threshold = NULL,
  direction = NULL,
  strata = NULL,
  strata.weight = NULL
)
```

Arguments

data   A data frame with each row representing a participant. The columns should be
                orders as:

- `ID`: Participant ID, must be numeric and unique.
- `Treatment Group Indicator`: 1 (True) = Treatment, 0 (False) = Control.
- `Outcome 1`: Observed outcome 1 in numeric format.
- `Censor Status of Outcome 1`: 1 (True) = Censored, 0 (False) = Not Censored.
- `Outcome 2`: Observed outcome 2 in numeric format.

- Censor Status of Outcome 2: 1 (True) = Censored, 0 (False) = Not Censored.
- similar for outcome 3, 4, and more.

method   Method used to obtain adaptive thresholds. "weights" or "calipers" as detailed below.

weights   A numeric vector indicates the weights when method "weights" is employed. Default to 1 for all outcomes.

calipers   A numeric value (or vector) indicates the calipers.

                    For method="weights", a single value that will be applied to all outcomes. Default to 0.2.

                    For method="calipers", a vector that contains calipers for each outcome. Input required for method="calipers".

clinical.threshold

                    A numeric vector represents the minimal clinical thresholds. Default to 0 for all endpoints.

direction   A numeric vector the more favorable results of each outcome. 1 for favoring larger outcome values (e.g., surviving longer time) and -1 for favoring smaller outcome values (e.g., having fewer adverse events).

strata   A numeric vector indicates the stratum that each participant belongs to. Only needed for analysis with stratification. Default to leaving blank for non-stratified analysis.

strata.weight   A data frame indicates weights of each stratum. Default to weighting base on numbers of participants within strata. If specified, the columns should be orders as:

- stratum: Stratum index, should be numeric, unique and corresponds to strata.
- weight: Weight for each stratum, should be numeric.

Value

A list of analysis results:

WR A numeric value. Estimated win ratio for treatment versus control.

P A numeric value. Two-sided P value of the Finkelstein-Schoenfeld (FS) test.

Stage.decompose A list of stage-level comparison results for each stratum. Each stratum corresponds to a matrix. A single matrix will be returned for non-stratified analysis for simplicity. The decomposition matrix presents proportions of wins, ties, and losses (obtained by the treatment group) at each stage. Proportions are always obtained with respect to the total number of comparisons between treatment and control groups.

strata.summary A data frame presents strata weights and stratum-specific WR results.

FS.stat A numeric value of the FS test statistic.

FS.stat.var A numeric value of the variance of the FS test statistic.

Examples

```
# Example 1: stratified WRAT analysis with two time-to-event endpoints.
#   The "weights" method employed.
analysis.results <- WRAT(data = sample_data[,1:6],
                         method = "weights",
```

```
                              weights = c(1,1), calipers = 0.2,
                              clinical.threshold = c(0,0),
                              direction = c(1,1),
                              strata = sample_data$strata,
                              strata.weight = NULL)
cat("WR:",analysis.results$WR, "; P-value:", analysis.results$P,"\n")

# Example 2: stratified WRAT analysis with two time-to-event endpoints.
#   The "calipers" method employed.
analysis.results <- WRAT(data = sample_data[,1:6],
                              method = "calipers",
                              weights = NULL, calipers = c(0.2,0.3),
                              clinical.threshold = c(0,0),
                              direction = c(1,1),
                              strata = sample_data$strata,
                              strata.weight = NULL)
cat("WR:",analysis.results$WR, "; P-value:", analysis.results$P,"\n")

# Example 3: non-stratified WRAT analysis with two time-to-event endpoints.
#   The "weights" method employed.
analysis.results <- WRAT(data = sample_data[,1:6],
                              method = "weights",
                              weights = c(1,1), calipers = 0.2,
                              clinical.threshold = c(0,0),
                              direction = c(1,1),
                              strata = NULL,
                              strata.weight = NULL)
cat("WR:",analysis.results$WR, "; P-value:", analysis.results$P,"\n")
```

WRAT.comparison   *Pairwise comparisons for WRAT*

Description

This function performs pairwise comparisons for WRAT analysis. To be called by function `WRAT()`.

Usage

```
WRAT.comparison(
  data,
  pair.data.list,
  threshold,
  stage = NULL,
  direction = NULL,
  strata = NULL,
  strata.weight = NULL
)
```

Arguments

data   A data frame with each row representing a participant. The columns should be
                orders as:

                • ID: Participant ID, must be numeric and unique.

- Treatment Group Indicator: 1 (True) = Treatment, 0 (False) = Control.
- Outcome 1: Observed outcome 1 in numeric format.
- Censor Status of Outcome 1: 1 (True) = Censored, 0 (False) = Not Censored.
- Outcome 2: Observed outcome 2 in numeric format.
- Censor Status of Outcome 2: 1 (True) = Censored, 0 (False) = Not Censored.
- similar for outcome 3, 4, and more.

pair.data.list   A list of data frames organized for stratified pairwise comparisons.

threshold   A numeric vector indicating thresholds for each stage.

stage   A numeric vector indicating the outcome measure considered at each stage of comparison (1 for outcome 1, 2 for outcome 2, etc.). If specified, the length must be the same with the length of threshold parameter. Default to alternating across outcomes when the length of threshold is a multiply of number of outcomes. E.g., with two outcomes and four thresholds specified, the default stage is (1,2,1,2).

direction   A numeric vector the more favorable results of each outcome. 1 for favoring larger outcome values (e.g., surviving longer time) and -1 for favoring smaller outcome values (e.g., having fewer adverse events). efault to favoring larger values for all outcomes.

strata   A numeric vector indicates the stratum that each participant belongs to. Only needed for analysis with stratification. Default to leaving blank for non-stratified analysis.

strata.weight   A data frame indicates weights of each stratum. Default to weighting base on numbers of participants within strata. If specified, the columns should be orders as:

- stratum: Stratum index, should be numeric, unique and corresponds to strata.
- weight: Weight for each stratum, should be numeric.

Value

A list of comparison results:

pair.data.list A list that contains data frames of pairwise comparison results and data used for comparison. Each stratum corresponds to one data frame.

stage.results.list A list that contains matrices of comparison results of each stage. Each stratum corresponds to one matrix. 1 for win, -1 for loss, 0 for tie, and NA for results determined by previous stages.

treatment A numeric vector indicates the treatment status.

strata A numeric vector indicates the stratum that each participant belongs to.

strata.weight A data frame contains weighting information for stratification analysis.

WRMT   *WRMT Analysis*

Description

Perform WRMT (win ratio with multiple thresholds) analysis.

Usage

```
WRMT(
  data,
  threshold,
  stage = NULL,
  direction = NULL,
  strata = NULL,
  strata.weight = NULL
)
```

Arguments

data
: A data frame with each row representing a participant. The columns should be orders as:

  - `ID`: Participant ID, must be numeric and unique.
  - `Treatment Group Indicator`: 1 (True) = Treatment, 0 (False) = Control.
  - `Outcome 1`: Observed outcome 1 in numeric format.
  - `Censor Status of Outcome 1`: 1 (True) = Censored, 0 (False) = Not Censored.
  - `Outcome 2`: Observed outcome 2 in numeric format.
  - `Censor Status of Outcome 2`: 1 (True) = Censored, 0 (False) = Not Censored.
  - similar for outcome 3, 4, and more.

threshold
: A numeric vector indicating thresholds for each stage.

stage
: A numeric vector indicating the outcome measure considered at each stage of comparison (1 for outcome 1, 2 for outcome 2, etc.). If specified, the length must be the same with the length of threshold parameter. Default to alternating across outcomes when the length of threshold is a multiply of number of outcomes. E.g., with two outcomes and four thresholds specified, the default stage is (1,2,1,2).

direction
: A numeric vector the more favorable results of each outcome. 1 for favoring larger outcome values (e.g., surviving longer time) and -1 for favoring smaller outcome values (e.g., having fewer adverse events). efault to favoring larger values for all outcomes.

strata
: A numeric vector indicates the stratum that each participant belongs to. Only needed for analysis with stratification. Default to leaving blank for non-stratified analysis.

strata.weight
: A data frame indicates weights of each stratum. Default to weighting base on numbers of participants within strata. If specified, the columns should be orders as:

- stratum: Stratum index, should be numeric, unique and corresponds to strata.
- weight: Weight for each stratum, should be numeric.

Value

A list of analysis results:

WR A numeric value. Estimated win ratio for treatment versus control.

P A numeric value. Two-sided P value of the Finkelstein-Schoenfeld (FS) test.

Stage.decompose A list of stage-level comparison results for each stratum. Each stratum corresponds to a matrix. A single matrix will be returned for non-stratified analysis for simplicity. The decomposition matrix presents proportions of wins, ties, and losses (obtained by the treatment group) at each stage. Proportions are always obtained with respect to the total number of comparisons between treatment and control groups.

strata.summary A data frame presents strata weights and stratum-specific WR results.

FS.stat A numeric value of the FS test statistic.

FS.stat.var A numeric value of the variance of the FS test statistic.

Examples

```
# Example 1: stratified WRMT analysis with two time-to-event endpoints.
#   Stages: endpoint 1 with threshold 10, endpoint 2 with threshold 7,
#   endpoint 1 with thresholds 0, and endpoint 2 with threshold 0.
#   That is stratified WRMT(10,7,0,0) analysis.

analysis.results <- WRMT(data = sample_data[,1:6],
                         threshold = c(0,0), stage = c(1,2),
                         direction = c(1,1),
                         strata = NULL,
                         strata.weight = NULL)
cat("WR:",analysis.results$WR, "; P-value:", analysis.results$P,"\n")


# Example 2: non-stratified WRMT analysis with two time-to-event endpoints.
#   Stages: endpoint 1 with threshold 10, endpoint 2 with threshold 7,
#   endpoint 1 with thresholds 0, and endpoint 2 with threshold 0.
#   That is non-stratified WRMT(10,7,0,0) analysis.

analysis.results <- WRMT(data = sample_data[,1:6],
                         threshold = c(0,0), stage = c(1,2),
                         direction = c(1,1),
                         strata = NULL,
                         strata.weight = NULL)
cat("WR:",analysis.results$WR, "; P-value:", analysis.results$P,"\n")

# Example 3: stratified standard Win Ratio analysis with
#   two time-to-event endpoints
analysis.results <- WRMT(data = sample_data[,1:6],
                         threshold = c(0,0), stage = c(1,2),
                         direction = c(1,1),
                         strata = sample_data$strata,
                         strata.weight = NULL)
cat("WR:",analysis.results$WR, "; P-value:", analysis.results$P,"\n")
```

```
# Example 4: non-stratified standard Win Ratio analysis with
#   two time-to-event endpoints
analysis.results <- WRMT(data = sample_data[,1:6],
                        threshold = c(0,0), stage = c(1,2),
                        direction = c(1,1),
                        strata = NULL,
                        strata.weight = NULL)
cat("WR:",analysis.results$WR, "; P-value:", analysis.results$P,"\n")
```

WRMT.comparison   *Pairwise comparisons for WRAT*

Description

This function performs pairwise comparisons for WRMT analysis. To be called by function WRMT().

Usage

```
WRMT.comparison(
  data,
  threshold,
  stage = NULL,
  direction = NULL,
  strata = NULL,
  strata.weight = NULL
)
```

Arguments

data
: A data frame with each row representing a participant. The columns should be orders as:
  - ID: Participant ID, must be numeric and unique.
  - Treatment Group Indicator: 1 (True) = Treatment, 0 (False) = Control.
  - Outcome 1: Observed outcome 1 in numeric format.
  - Censor Status of Outcome 1: 1 (True) = Censored, 0 (False) = Not Censored.
  - Outcome 2: Observed outcome 2 in numeric format.
  - Censor Status of Outcome 2: 1 (True) = Censored, 0 (False) = Not Censored.
  - similar for outcome 3, 4, and more.

threshold
: A numeric vector indicating thresholds for each stage.

stage
: A numeric vector indicating the outcome measure considered at each stage of comparison (1 for outcome 1, 2 for outcome 2, etc.). If specified, the length must be the same with the length of threshold parameter. Default to alternating across outcomes when the length of threshold is a multiply of number of outcomes. E.g., with two outcomes and four thresholds specified, the default stage is (1,2,1,2).

direction   A numeric vector the more favorable results of each outcome. 1 for favoring
                   larger outcome values (e.g., surviving longer time) and -1 for favoring smaller
                   outcome values (e.g., having fewer adverse events). efault to favoring larger
                   values for all outcomes.

strata   A numeric vector indicates the stratum that each participant belongs to. Only
                   needed for analysis with stratification. Default to leaving blank for non-stratified
                   analysis.

strata.weight   A data frame indicates weights of each stratum. Default to weighting base on
                   numbers of participants within strata. If specified, the columns should be orders
                   as:

                      • stratum: Stratum index, should be numeric, unique and corresponds to
                        strata.
                      • weight: Weight for each stratum, should be numeric.

Value

A list of comparison results:

pair.data.list A list that contains data frames of pairwise comparison results and data used for
   comparison. Each stratum corresponds to one data frame.

stage.results.list A list that contains matrices of comparison results of each stage. Each stratum
   corresponds to one matrix. 1 for win, -1 for loss, 0 for tie, and NA for results determined by
   previous stages.

treatment A numeric vector indicates the treatment status.

strata A numeric vector indicates the stratum that each participant belongs to.

strata.weight A data frame contains weighting information for stratification analysis.

Examples

```
# Example 1: stratified comparison
strata.compare <- WRMT.comparison(data = sample_data[,1:6],
                                  threshold = c(0,0), stage = c(1,2),
                                  direction = c(1,1),
                                  strata = sample_data$strata,
                                  strata.weight = NULL)

# Example 2: non-stratified comparison
nonstrata.compare <- WRMT.comparison(data = sample_data[,1:6],
                                     threshold = c(0,0), stage = c(1,2),
                                     direction = c(1,1),
                                     strata.weight = NULL)
```

WRMT.one.stage.sur   *Comparison for a single stage with potential right censoring*

Description

Comparison for a single stage with potential right censoring

Usage

```
WRMT.one.stage.sur(t1, t2, c1, c2, threshold)
```

Arguments

t1	A numeric vector. Observed outcome for target participants.
t2	A numeric vector. Observed outcome for participants for comparison.
c1	A numeric vector. Censoring indicator for target participants.
c2	A numeric vector. Censoring indicator for participants for comparison.
threshold	A numeric value. Threshold used for comparison at this stage, differences smaller than this threshold are considered undetermined.

Value

A numeric vector that indicates the comparison results for this stage: 1 for wins by target participants, -1 for losses by target participants, and 0 for undetermined pairs.

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