Package ‘metaRMST’

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Title Meta-Analysis of RMSTD
Version 1.0.0
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URL https://github.com/iweir/metaRMST
Description R implementation of a multivariate meta-analysis of randomized controlled trials (RCT) with the difference in restricted mean survival times (RMSTD). Use this package with individual patient level data from an RCT for a time-to-event outcome to determine combined effect estimates according to 4 methods: 1) a univariate meta-analysis using observed treatment effects, 2) a univariate meta-analysis using effects predicted by fitted Royston-Parmar flexible parametric models, 3) multivariate meta-analysis with analytically derived covariance, 4) multivariate meta-analysis with bootstrap derived covariance. This package computes all combined effects and provides an RMSTD curve with combined effect estimates and their confidence intervals.
Depends R (>= 3.4.0), rstpm2
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AorticStenosisTrials  Aortic Stenosis RCT data

Description

Data from 5 randomized controlled trials of transcatheter aortic valve replacement vs surgery in patients with Aortic Stenosis. The outcome is time until death from any cause. For each RCT, we reconstructed the individual patient data for each randomization group. We first extracted the time and survival probability coordinates from the Kaplan-Meier curves using the DigitizeIt software (http://www.digitizeit.de/). We used these coordinates, the total numbers of events, and the numbers of participants at risk to determine individual event times and event indicators. (Guyot, BMC Med Res Method 2012)

Usage

data(AorticStenosisTrials)

Format

An object of class data.frame with 5417 rows and 4 columns.

Note

<table>
<thead>
<tr>
<th>Trial ID</th>
<th>Trial Name</th>
<th>Last observed time (months)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NOTION</td>
<td>24.0</td>
</tr>
<tr>
<td>2</td>
<td>PARTNER</td>
<td>63.3</td>
</tr>
<tr>
<td>3</td>
<td>SURTAVI</td>
<td>24.1</td>
</tr>
<tr>
<td>4</td>
<td>PARTNER2</td>
<td>36.1</td>
</tr>
<tr>
<td>5</td>
<td>USCoreValve</td>
<td>24.1</td>
</tr>
</tbody>
</table>

* minimum of the last observed times across the two randomization groups.

References


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### Description

Perform a meta-analysis with RMSTD using individual patient data. Methods include:

1. "mvma" a multivariate meta-analysis borrowing strength across time-points with within-trial covariance matrix derived analytically
2. "mvma_boot" a multivariate meta-analysis borrowing strength across time-points with within-trial covariance matrix derived by bootstrap
3. "uni" a univariate meta-analysis for combined effect at each time-point using only available data
4. "uni_flex" a univariate meta-analysis for combined effect at each time-point using estimates based on flexible parametric models as described by Wei et al (Stat Med 2015).

### Usage

```
metaRMSTD(trialdata, time_horizons, MA_method, nboot = 500)
```

### Arguments

- **trialdata**
  - IPD trial data, see details for specifications
- **time_horizons**
  - specified vector of time horizons for the meta-analysis
- **MA_method**
  - the desired meta-analysis method; options are: "mvma", "mvma_boot", "uni", "uni_flex"
- **nboot**
  - the number of bootstrap iterations, if using the MVMA with bootstrap covariance matrix; default=500

### Details

Specify the time horizons at which to calculate the meta-analytic results. The trialdata must be formatted as a dataframe containing the IPD for each single trial. Variable names must include Trial ID ("trialID"), Time ("Time"), Event status ("Event"), and randomization group ("Arm").
Value

The \texttt{metaRMSTD} function returns a list object containing the random-effects model results, the \textit{RMSTD} and SE values for each trial at each available time horizon, and the estimated within-trial covariance matrix for each RCT.

Note

\textit{RMSTD} is estimable if time horizon > minimum of last observed times across the two groups. We implement the method-of-moments estimator for MVMA (Chen et al. Biometrics 2012, Jackson et al. Biometrical Journ 2013) and Dersimonian and Laird for univariate MA.

References


Examples

```r
# read in built-in dataset
data(AorticStenosisTrials)

# meta-analysis to obtain combined effect by multivariate model (method="mvma")
result <- metaRMSTD(AorticStenosisTrials, time_horizons=c(12,24,36), MA_method="mvma")

# generate figure:
obj <- RMSTcurves(AorticStenosisTrials, time_horizons=c(12,24,36), tmax=40, nboot=500)
RMSTplot(obj, xlim=c(0,40), ylim=c(-0.25,2.75), yby=0.5, ylab="RMSTD (mos)", xlab="Time (mos)")
```

Description

Prepare the data for use with \texttt{RMSTplot}. This function computes \textit{RMSTD} over specified time horizons and also fits a flexible parametric model to each trial. It calls the \texttt{metaRMSTD} function to compute the estimated combined effects for each of the 4 methods.
Usage

RMSTcurves(trialdata, time_horizons, tmax = max(time_horizons),
  tstep = 0.25, nboot = 500, MA_mvma = TRUE, MA_mvma_boot = TRUE,
  MA_uni = TRUE, MA_uni_flex = TRUE)

Arguments

  trialdata         IPD trial data
  time_horizons    specified vector of time horizons for the meta-analysis
  tmax             maximum value for RMSTD to be calculated in each trial
  tstep            increment for calculation of RMSTD over time interval from 0 to tmax; de-
                    fault=0.25
  nboot            the number of bootstrap iterations, if using the MVMA with bootstrap covari-
                    ance matrix; default=500
  MA_mvma          TRUE or FALSE indicates whether to include combined effect by this method
  MA_mvma_boot     TRUE or FALSE indicates whether to include combined effect by this method
  MA_uni           TRUE or FALSE indicates whether to include combined effect by this method
  MA_uni_flex      TRUE or FALSE indicates whether to include combined effect by this method

Value

an object to be plotted with RMSTplot

References

Royston, P. and Parmar, MK. Flexible parametric proportional-hazards and proportional-odds mod-
els for censored survival data, with application to prognostic modelling and estimation of treatment

Description

Plot RMST curves in each trial and combined effects

Usage

RMSTplot(RMSTobject, type = "l", col = c("red", "blue", "green",
  "orange", "purple", "yellow", "brown", "gray"), lwd = 2,
  ylim = c(-0.75, 2.75), yby = 0.25, xlim = c(0, 36), xby = 12,
  main = "", xlab = "Time (unit)",
  ylab = "Difference in RMST (unit)", trial_legend = TRUE,
  MA_legend = TRUE, estimates = TRUE)
Arguments

RMSTobject  object created by RMSTcurves

<table>
<thead>
<tr>
<th>Option</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>type</td>
<td>specify plot type (defaults to line plot)</td>
</tr>
<tr>
<td>col</td>
<td>option to specify vector of colors for each study</td>
</tr>
<tr>
<td>lwd</td>
<td>option to specify line width</td>
</tr>
<tr>
<td>ylim</td>
<td>option to specify limits for y axis</td>
</tr>
<tr>
<td>yby</td>
<td>option to specify intervals for y axis</td>
</tr>
<tr>
<td>xlim</td>
<td>option to specify limits for x axis</td>
</tr>
<tr>
<td>xby</td>
<td>option to specify intervals for x axis</td>
</tr>
<tr>
<td>main</td>
<td>option to add title</td>
</tr>
<tr>
<td>xlab</td>
<td>option to specify x axis label</td>
</tr>
<tr>
<td>ylab</td>
<td>option to specify y axis label</td>
</tr>
<tr>
<td>trial_legend</td>
<td>option to include a legend for trial colors</td>
</tr>
<tr>
<td>MA_legend</td>
<td>option to include a legend for meta-analysis symbols</td>
</tr>
<tr>
<td>estimates</td>
<td>option to include meta-analysis estimates and CIs</td>
</tr>
</tbody>
</table>

Value

a plot of RMSTD over time with option to add combined effect estimates and pointwise 95
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