# Package 'landest'

November 15, 2015

**Type** Package

**Title** Landmark Estimation of Survival and Treatment Effect

**Version** 1.0

**Date** 2015-11-08

**Author** Layla Parast

**Maintainer** Layla Parast <parast@rand.org>

**Description** Provides functions to estimate survival and a treatment effect using a landmark estimation approach.

**License** GPL

**Imports** stats, survival

**NeedsCompilation** no

**Repository** CRAN

**Date/Publication** 2015-11-15 10:09:05

## R topics documented:

| landest-package | *Survival and treatment effect estimation* |
|---|---|

### Description

Provides functions to estimate the probability of survival past some specified time and the treatment effect, defined as the difference in survival at the specified time, using Kaplan-Meier estimation, landmark estimation for a randomized trial setting, inverse probability of treatment weighted (IPTW) Kaplan-Meier estimation, and landmark estimation for an observational study setting. The landmark estimation approaches provide improved efficiency by incorporating intermediate event information and are robust to model misspecification. The IPTW Kaplan-Meier approach and landmark estimation in an observational study setting approach account for potential selection bias.

### Details

|  |  |
|---|---|
| Package: | landest |
| Type: | Package |
| Version: | 1.0 |
| Date: | 2015-11-08 |
| License: | GPL |

### Author(s)

Layla Parast

Maintainer: Layla Parast <parast@rand.org>

### References

Kaplan, E. L., & Meier, P. (1958). Nonparametric estimation from incomplete observations. Journal of the American Statistical Association, 53(282), 457-481.

Xie, J., & Liu, C. (2005). Adjusted Kaplan-Meier estimator and log-rank test with inverse probability of treatment weighting for survival data. Statistics in Medicine, 24(20), 3089-3110.

Parast, L., Tian, L., & Cai, T. (2014). Landmark Estimation of Survival and Treatment Effect in a Randomized Clinical Trial. Journal of the American Statistical Association, 109(505), 384-394.

Parast, L. & Griffin B.A. (2015). Landmark Estimation of Survival and Treatment Effects in Observational Studies, in press.

### Examples

```
data(example_rct)
delta.km(tl=example_rct$TL, dl = example_rct$DL, treat = example_rct$treat, tt=2)
#executable but takes time
```

```
#delta.land.rct(tl=example_rct$TL, dl = example_rct$DL, treat = example_rct$treat, tt=2,
#landmark = 1, short = cbind(example_rct$TS,example_rct$DS), z.cov = as.matrix(example_rct$Z))
data(example_obs)
delta.iptw.km(tl=example_obs$TL, dl = example_obs$DL, treat = example_obs$treat, tt=2,
cov.for.ps = as.matrix(example_obs$Z))
#executable but takes time
#delta.land.obs(tl=example_obs$TL, dl = example_obs$DL, treat = example_obs$treat, tt=2,
#landmark = 1, short = cbind(example_obs$TS,example_obs$DS), z.cov = as.matrix(example_obs$Z),
#cov.for.ps = as.matrix(example_obs$Z))
```

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| delta.iptw.km | *Estimates survival and treatment effect using inverse probability of treatment weighted (IPTW) Kaplan-Meier estimation* |
|---|---|

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## Description

Estimates the probability of survival past some specified time and the treatment effect, defined as the difference in survival at the specified time, using inverse probability of treatment weighted (IPTW) Kaplan-Meier estimation

## Usage

```
delta.iptw.km(tl, dl, treat, tt, var = FALSE, conf.int = FALSE, ps.weights = NULL,
weight.perturb = NULL, perturb.ps = FALSE, cov.for.ps = NULL)
```

## Arguments

| | |
|---|---|
| tl | observed event time of primary outcome, equal to min(T, C) where T is the event time and C is the censoring time. |
| dl | event indicator, equal to I(T<C) where T is the event time and C is the censoring time. |
| treat | treatment indicator, should be 0/1. |
| tt | the time of interest, function estimates the probability of survival past this time |
| var | TRUE or FALSE; indicates whether variance estimates for the treatment effect and survival in each group are requested, default is FALSE. |
| conf.int | TRUE or FALSE; indicates whether 95% confidence intervals for the treatment effect and survival in each group are requested, default is FALSE. |
| ps.weights | propensity score (or inverse probability of treatment) weights |
| weight.perturb | a (n1+n0) by x matrix of weights where n1 = length of tl for treatment group 1 and n0 = length of tl for treatment group 0; used for perturbation-resampling, default is null. If var or conf.int is TRUE and weight.perturb is not provided, the function generates exponential(1) weights. |
| perturb.ps | TRUE or FALSE indicating whether the weight.perturb matrix includes the perturbed propensity score (or inverse probability of treatment) weights; if cov.for.ps is supplied instead of ps.weights, this is forced to be TRUE. |
| cov.for.ps | matrix of covariates to be used to estimate propensity score (or inverse probability of treatment) weights; either ps.weights or cov.for.ps must be supplied. |

## Details

Let $T_{Li}$ denote the time of the primary event of interest for person $i$, $C_i$ denote the censoring time, $Z_i$ denote the vector of baseline (pretreatment) covariates, and $G_i$ be the treatment group indicator such that $G_i = 1$ indicates treatment and $G_i = 0$ indicates control. Due to censoring, we observe $X_{Li} = min(T_{Li}, C_i)$ and $\delta_{Li} = I(T_{Li} \leq C_i)$. This function estimates survival at time t within each treatment group, $S_j(t) = P(T_L > t|G = j)$ for $j = 1, 0$ and the treatment effect defined as $\Delta(t) = S_1(t) - S_0(t)$.

The inverse probability of treatment weighted (IPTW) Kaplan-Meier (KM) estimate of survival at time t for each treatment group is

$$\hat{S}_{IPTW,KM,j}(t) = \prod_{t_{kj} \leq t} \left[ 1 - \frac{d_{kj}^w}{y_{kj}^w} \right] \text{ if } t \geq t_{1j}, \text{ or } 1 \text{ if } t < t_{1j}$$

where $t_{1j}, ..., t_{Dj}$ are the distinct observed event times of the primary outcome in treatment group j, $d_{kj}^w = \sum_{i:X_{Li}=t_{kj},\delta_{Li}=1} \hat{W}_j(Z_i)^{-1} \delta_{Li} I(G_i = j)$ and $y_{kj}^w = \sum_{i:X_{Li} \geq t_{kj}} \hat{W}_j(Z_i)^{-1} I(G_i = j)$, $W_j(Z_i) = P(G_i = j|Z_i)$, and $\hat{W}_j(Z_i)$ is the estimated propensity score (see ps.wgt.fun for more information). The IPTW KM estimate of treatment effect at time t is $\hat{\Delta}_{IPTW,KM}(t) = \hat{S}_{IPTW,KM,1}(t) - \hat{S}_{IPTW,KM,0}(t)$.

To obtain variance estimates and construct confidence intervals, we use a perturbation-resampling method. Specifically, let $\{V^{(b)} = (V_1^{(b)}, ..., V_n^{(b)})^T, b = 1, ...B\}$ be $n \times B$ independent copies of a positive random variable U from a known distribution with unit mean and unit variance such as an Exp(1) distribution. To estimate the variance of our estimates, we appropriately weight the estimates using these perturbation weights to obtain perturbed values: $\hat{S}_{IPTW,KM,0}(t)^{(b)}$, $\hat{S}_{IPTW,KM,1}(t)^{(b)}$, and $\hat{\Delta}_{IPTW,KM}(t)^{(b)}, b = 1, ...B$. We then estimate the variance of each estimate as the empirical variance of the perturbed quantities. To construct confidence intervals, one can either use the empirical percentiles of the perturbed samples or a normal approximation.

## Value

A list is returned:

| | |
|---|---|
| S.estimate.1 | the estimate of survival at the time of interest for treatment group 1, $\hat{S}_1(t) = P(T > t|G = 1)$ |
| S.estimate.0 | the estimate of survival at the time of interest for treatment group 0, $\hat{S}_0(t) = P(T > t|G = 0)$ |
| delta.estimate | the estimate of treatment effect at the time of interest |
| S.var.1 | the variance estimate of $\hat{S}_1(t)$; if var = TRUE or conf.int = TRUE |
| S.var.0 | the variance estimate of $\hat{S}_0(t)$; if var = TRUE or conf.int = TRUE |
| delta.var | the variance estimate of $\hat{\Delta}(t)$; if var = TRUE or conf.int = TRUE |
| p.value | the p-value from testing $\Delta(t) = 0$; if var = TRUE or conf.int = TRUE |
| conf.int.normal.S.1 | a vector of size 2; the 95% confidence interval for $\hat{S}_1(t)$ based on a normal approximation; if conf.int = TRUE |

conf.int.normal.S.0

> a vector of size 2; the 95% confidence interval for $\hat{S}_0(t)$ based on a normal approximation; if conf.int = TRUE

conf.int.normal.delta

> a vector of size 2; the 95% confidence interval for $\hat{\Delta}(t)$ based on a normal approximation; if conf.int = TRUE

conf.int.quantile.S.1

> a vector of size 2; the 95% confidence interval for $\hat{S}_1(t)$ based on sample quantiles of the perturbed values, described above; if conf.int = TRUE

conf.int.quantile.S.0

> a vector of size 2; the 95% confidence interval for $\hat{S}_0(t)$ based on sample quantiles of the perturbed values, described above; if conf.int = TRUE

conf.int.quantile.delta

> a vector of size 2; the 95% confidence interval for $\hat{\Delta}(t)$ based on sample quantiles of the perturbed values, described above; if conf.int = TRUE

## Author(s)

Layla Parast

## References

Xie, J., & Liu, C. (2005). Adjusted Kaplan-Meier estimator and log-rank test with inverse probability of treatment weighting for survival data. Statistics in Medicine, 24(20), 3089-3110.

Rosenbaum, P. R., & Rubin, D. B. (1983). The central role of the propensity score in observational studies for causal effects. Biometrika, 70(1), 41-55.

Rosenbaum, P. R., & Rubin, D. B. (1984). Reducing bias in observational studies using subclassification on the propensity score. Journal of the American Statistical Association, 79(387), 516-524.

## Examples

```
data(example_obs)
W.weight = ps.wgt.fun(treat = example_obs$treat, cov.for.ps = as.matrix(example_obs$Z))
delta.iptw.km(tl=example_obs$TL, dl = example_obs$DL, treat = example_obs$treat, tt=2,
ps.weights = W.weight)
delta.iptw.km(tl=example_obs$TL, dl = example_obs$DL, treat = example_obs$treat, tt=2,
cov.for.ps = as.matrix(example_obs$Z))
```

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| delta.km | *Estimates survival and treatment effect using Kaplan-Meier estimation* |

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## Description

Estimates the probability of survival past some specified time and the treatment effect, defined as the difference in survival at the specified time, using Kaplan-Meier estimation

## Usage

```
delta.km(tl, dl, treat, tt, var = FALSE, conf.int = FALSE, weight.perturb = NULL)
```

## Arguments

| | |
|---|---|
| `tl` | observed event time of primary outcome, equal to min(T, C) where T is the event time and C is the censoring time. |
| `dl` | event indicator, equal to I(T<C) where T is the event time and C is the censoring time. |
| `treat` | treatment indicator, should be 0/1. |
| `tt` | the time of interest, function estimates the probability of survival past this time |
| `var` | TRUE or FALSE; indicates whether variance estimates for the treatment effect and survival in each group are requested, default is FALSE. |
| `conf.int` | TRUE or FALSE; indicates whether 95% confidence intervals for the treatment effect and survival in each group are requested, default is FALSE. |
| `weight.perturb` | a (n1+n0) by x matrix of weights where n1 = length of tl for treatment group 1 and n0 = length of tl for treatment group 0; used for perturbation-resampling, default is null. If var or conf.int is TRUE and weight.perturb is not provided, the function generates exponential(1) weights. |

## Details

Let $T_{Li}$ denote the time of the primary event of interest for person $i$, $C_i$ denote the censoring time and $G_i$ be the treatment group indicator such that $G_i = 1$ indicates treatment and $G_i = 0$ indicates control. Due to censoring, we observe $X_{Li} = min(T_{Li}, C_i)$ and $\delta_{Li} = I(T_{Li} \leq C_i)$. This function estimates survival at time t within each treatment group, $S_j(t) = P(T_L > t | G = j)$ for $j = 1, 0$ and the treatment effect defined as $\Delta(t) = S_1(t) - S_0(t)$.

The Kaplan-Meier (KM) estimate of survival at time t for each treatment group is

$$\hat{S}_{KM,j}(t) = \prod_{t_{kj} \leq t} \left[ 1 - \frac{d_{kj}}{y_{kj}} \right] \text{ if } t \geq t_{1j}, \text{ or } 1 \text{ if } t < t_{1j}$$

where $t_{1j}, ..., t_{Dj}$ are the distinct observed event times of the primary outcome in treatment group j, $d_{kj}$ is the number of events at time $t_{kj}$ in treatment group j, and $y_{kj}$ is the number of patients at risk at $t_{kj}$ in treatment group j. The Kaplan-Meier (KM) estimate of treatment effect at time t is $\hat{\Delta}_{KM}(t) = \hat{S}_{KM,1}(t) - \hat{S}_{KM,0}(t)$.

To obtain variance estimates and construct confidence intervals, we use a perturbation-resampling method. Specifically, let $\{V^{(b)} = (V_1^{(b)}, ..., V_n^{(b)})^T, b = 1, ...B\}$ be $n \times B$ independent copies of a positive random variable U from a known distribution with unit mean and unit variance such as an Exp(1) distribution. To estimate the variance of our estimates, we appropriately weight the estimates using these perturbation weights to obtain perturbed values: $\hat{S}_{KM,0}(t)^{(b)}$, $\hat{S}_{KM,1}(t)^{(b)}$, and $\hat{\Delta}_{KM}(t)^{(b)}, b = 1, ...B$. We then estimate the variance of each estimate as the empirical variance of the perturbed quantities. To construct confidence intervals, one can either use the empirical percentiles of the perturbed samples or a normal approximation.

**Value**

A list is returned:

| | |
|---|---|
| S.estimate.1 | the estimate of survival at the time of interest for treatment group 1, $\hat{S}_1(t) = P(T > t|G = 1)$ |
| S.estimate.0 | the estimate of survival at the time of interest for treatment group 0, $\hat{S}_0(t) = P(T > t|G = 0)$ |
| delta.estimate | the estimate of treatment effect at the time of interest |
| S.var.1 | the variance estimate of $\hat{S}_1(t)$; if var = TRUE or conf.int = TRUE |
| S.var.0 | the variance estimate of $\hat{S}_0(t)$; if var = TRUE or conf.int = TRUE |
| delta.var | the variance estimate of $\hat{\Delta}(t)$; if var = TRUE or conf.int = TRUE |
| p.value | the p-value from testing $\Delta(t) = 0$; if var = TRUE or conf.int = TRUE |
| conf.int.normal.S.1 | |
| | a vector of size 2; the 95% confidence interval for $\hat{S}_1(t)$ based on a normal approximation; if conf.int = TRUE |
| conf.int.normal.S.0 | |
| | a vector of size 2; the 95% confidence interval for $\hat{S}_0(t)$ based on a normal approximation; if conf.int = TRUE |
| conf.int.normal.delta | |
| | a vector of size 2; the 95% confidence interval for $\hat{\Delta}(t)$ based on a normal approximation; if conf.int = TRUE |
| conf.int.quantile.S.1 | |
| | a vector of size 2; the 95% confidence interval for $\hat{S}_1(t)$ based on sample quantiles of the perturbed values, described above; if conf.int = TRUE |
| conf.int.quantile.S.0 | |
| | a vector of size 2; the 95% confidence interval for $\hat{S}_0(t)$ based on sample quantiles of the perturbed values, described above; if conf.int = TRUE |
| conf.int.quantile.delta | |
| | a vector of size 2; the 95% confidence interval for $\hat{\Delta}(t)$ based on sample quantiles of the perturbed values, described above; if conf.int = TRUE |

**Author(s)**

Layla Parast

**References**

Kaplan, E. L., & Meier, P. (1958). Nonparametric estimation from incomplete observations. Journal of the American Statistical Association, 53(282), 457-481.

**Examples**

```
data(example_rct)
delta.km(tl=example_rct$TL, dl = example_rct$DL, treat = example_rct$treat, tt=2)
```

---

| delta.land.obs | *Estimates survival and treatment effect using landmark estimation* |
|---|---|

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### Description

Estimates the probability of survival past some specified time and the treatment effect, defined as the difference in survival at the specified time, using landmark estimation for an observational study setting

### Usage

```
delta.land.obs(tl, dl, treat, tt, landmark, short = NULL, z.cov = NULL,
var = FALSE, conf.int = FALSE, ps.weights = NULL, weight.perturb = NULL,
perturb.ps = FALSE, cov.for.ps = NULL, bw = NULL)
```

### Arguments

| | |
|---|---|
| tl | observed event time of primary outcome, equal to min(T, C) where T is the event time and C is the censoring time. |
| dl | event indicator, equal to I(T<C) where T is the event time and C is the censoring time. |
| treat | treatment indicator, should be 0/1. |
| tt | the time of interest, function estimates the probability of survival past this time |
| landmark | the landmark time |
| short | a matrix of intermediate event information, there should be two columns for each intermediate event, the first column contains the observed intermediate event time, equal to min(TS, C) where TS is the event time and C is the censoring time, and the second column contains the event indicator, equal to I(TS<C) |
| z.cov | matrix of baseline covariate information |
| var | TRUE or FALSE; indicates whether variance estimates for the treatment effect and survival in each group are requested, default is FALSE. |
| conf.int | TRUE or FALSE; indicates whether 95% confidence intervals for the treatment effect and survival in each group are requested, default is FALSE. |
| ps.weights | propensity score (or inverse probability of treatment) weights |
| weight.perturb | a (n1+n0) by x matrix of weights where n1 = length of tl for treatment group 1 and n0 = length of tl for treatment group 0; used for perturbation-resampling, default is null. If var or conf.int is TRUE and weight.perturb is not provided, the function generates exponential(1) weights. |
| perturb.ps | TRUE or FALSE indicating whether the weight.perturb matrix includes the perturbed propensity score (or inverse probability of treatment) weights; if cov.for.ps is supplied instead of ps.weights, this is forced to be TRUE. |
| cov.for.ps | matrix of covariates to be used to estimate propensity score (or inverse probability of treatment) weights; either ps.weights or cov.for.ps must be supplied. |
| bw | bandwidth used for kernel estimation, default is NULL |

## Details

Let $T_{Li}$ denote the time of the primary event of interest for person $i$, $T_{Si}$ denote the time of the available intermediate event(s), $C_i$ denote the censoring time, $Z_i$ denote the vector of baseline (pretreatment) covariates, and $G_i$ be the treatment group indicator such that $G_i = 1$ indicates treatment and $G_i = 0$ indicates control. Due to censoring, we observe $X_{Li} = min(T_{Li}, C_i)$ and $\delta_{Li} = I(T_{Li} \leq C_i)$ and $X_{Si} = min(T_{Si}, C_i)$ and $\delta_{Si} = I(T_{Si} \leq C_i)$. This function estimates survival at time t within each treatment group, $S_j(t) = P(T_L > t | G = j)$ for $j = 1, 0$ and the treatment effect defined as $\Delta(t) = S_1(t) - S_0(t)$.

To derive these estimates using landmark estimation for an observational study setting, we first decompose the quantity into two components $S_j(t) = S_j(t|t_0)S_j(t_0)$ using a landmark time $t_0$ and estimate each component separately incorporating inverse probability of treatment weights (IPTW) to account for potential selection bias. Let $W_j(Z_i) = P(G_i = j|Z_i)$, and $\hat{W}_j(Z_i)$ be the estimated propensity score (or probability of treatment, see ps.wgt.fun for more information). In this presentation, we assume $Z_i$ indicates the vector of baseline (pretreatment) covariates and that $Z_i$ is used to estimate the propensity scores and incorporated into the survival and treatment effect estimation. However, the function allows one to use different subsets of $Z_i$ for the propensity score estimation vs. survival estimation, as is appropriate in the setting of interest. Intermediate event information is used in estimation of the conditional component $S_j(t|t_0)$,

$$S_j(t|t_0) = P(T_L > t|T_L > t_0, G = j) = E[E[I(T_L > t|T_L > t_0, G = j, H)]] = E[S_{j,H}(t|t_0)]$$

where $S_{j,H}(t|t_0) = P(T_L > t|T_L > t_0, G = j, H)$ and $H = \{Z, I(T_S \leq t_0), min(T_S, t_0)\}$. Then $S_{j,H}(t|t_0)$ is estimated in two stages. The first stage involves fitting a weighted Cox proportional hazards model among individuals with $X_L > t_0$ to obtain an estimate of $\beta$, denoted as $\hat{\beta}$,

$$S_{j,H}(t|t_0) = \exp\{-\Lambda_{j,0}(t|t_0)\exp(\beta^T H)\}$$

where $\Lambda_{j,0}(t|t_0)$ is the cumulative baseline hazard in group $j$. Specifically, $\hat{\beta}$ is the solution to the weighted Cox partial likelihoodand, with weights $\hat{W}_j(Z_i)^{-1}$. The second stage uses a weighted nonparametric kernel Nelson-Aalen estimator to obtain a local constant estimator for the conditional hazard $\Lambda_{j,u}(t|t_0) = -\log[S_{j,u}(t|t_0)]$ as

$$\hat{\Lambda}_{j,u}(t|t_0) = \int_{t_0}^{t} \frac{\sum_i \hat{W}_j(Z_i)^{-1}K_h(\hat{U}_i - u)dN_i(z)}{\sum_i \hat{W}_j(Z_i)^{-1}K_h(\hat{U}_i - u)Y_i(z)}$$

where $S_{j,u}(t|t_0) = P(T_L > t|T_L > t_0, G = j, \hat{U} = u), \hat{U} = \hat{\beta}^T H, Y_i(t) = I(T_L \geq t), N_i(t) = I(T_L \leq t)I(T_L < C), K(\cdot)$ is a smooth symmetric density function, $K_h(x/h)/h$, $h = O(n^{-v})$ is a bandwidth with $1/2 > v > 1/4$, and the summation is over all individuals with $G = j$ and $X_L > t_0$. The resulting estimate for $S_{j,u}(t|t_0)$ is $\hat{S}_{j,u}(t|t_0) = \exp\{-\hat{\Lambda}_{j,u}(t|t_0)\}$, and the final estimate

$$\hat{S}_j(t|t_0) = \frac{n^{-1}\sum_{i=1}^{n}\hat{W}_j(Z_i)^{-1}\hat{S}_j(t|t_0, H_i)I(G_i = 1)I(X_{Li} > t_0)}{n^{-1}\sum_{i=1}^{n}\hat{W}_j(Z_i)^{-1}I(G_i = 1)I(X_{Li} > t_0)}$$

is a consistent estimate of $S_j(t|t_0)$.

Estimation of $S_j(t_0)$ uses a similar two-stage approach but using only baseline covariates, to obtain $\hat{S}_j(t_0)$. The final overall estimate of survival at time $t$ is, $\hat{S}_{LM,j}(t) = \hat{S}_j(t|t_0)\hat{S}_j(t_0)$. The treatment effect in terms of the difference in survival at time $t$ is estimated as $\hat{\Delta}_{LM}(t) = \hat{S}_{LM,1}(t) - \hat{S}_{LM,0}(t)$. To obtain an appropriate $h$ we first use the bandwidth selection procedure given by Scott(1992) to obtain $h_{opt}$; and then we let $h = h_{opt}n_j^{-0.10}$.

To obtain variance estimates and construct confidence intervals, we use a perturbation-resampling method. Specifically, let $\{V^{(b)} = (V_1^{(b)}, ..., V_n^{(b)})^T, b = 1, ...B\}$ be $n \times B$ independent copies of a positive random variable U from a known distribution with unit mean and unit variance such as an Exp(1) distribution. To estimate the variance of our estimates, we appropriately weight the estimates using these perturbation weights to obtain perturbed values: $\hat{S}_{LM,0}(t)^{(b)}$, $\hat{S}_{LM,1}(t)^{(b)}$, and $\hat{\Delta}_{LM}(t)^{(b)}, b = 1, ...B$. We then estimate the variance of each estimate as the empirical variance of the perturbed quantities. To construct confidence intervals, one can either use the empirical percentiles of the perturbed samples or a normal approximation.

**Value**

A list is returned:

S.estimate.1     the estimate of survival at the time of interest for treatment group 1, $\hat{S}_1(t) = P(T > t | G = 1)$

S.estimate.0     the estimate of survival at the time of interest for treatment group 0, $\hat{S}_0(t) = P(T > t | G = 0)$

delta.estimate    the estimate of treatment effect at the time of interest

S.var.1           the variance estimate of $\hat{S}_1(t)$; if var = TRUE or conf.int = TRUE

S.var.0           the variance estimate of $\hat{S}_0(t)$; if var = TRUE or conf.int = TRUE

delta.var        the variance estimate of $\hat{\Delta}(t)$; if var = TRUE or conf.int = TRUE

p.value           the p-value from testing $\Delta(t) = 0$; if var = TRUE or conf.int = TRUE

conf.int.normal.S.1

       a vector of size 2; the 95% confidence interval for $\hat{S}_1(t)$ based on a normal approximation; if conf.int = TRUE

conf.int.normal.S.0

       a vector of size 2; the 95% confidence interval for $\hat{S}_0(t)$ based on a normal approximation; if conf.int = TRUE

conf.int.normal.delta

       a vector of size 2; the 95% confidence interval for $\hat{\Delta}(t)$ based on a normal approximation; if conf.int = TRUE

conf.int.quantile.S.1

       a vector of size 2; the 95% confidence interval for $\hat{S}_1(t)$ based on sample quantiles of the perturbed values, described above; if conf.int = TRUE

conf.int.quantile.S.0

       a vector of size 2; the 95% confidence interval for $\hat{S}_0(t)$ based on sample quantiles of the perturbed values, described above; if conf.int = TRUE

conf.int.quantile.delta

       a vector of size 2; the 95% confidence interval for $\hat{\Delta}(t)$ based on sample quantiles of the perturbed values, described above; if conf.int = TRUE

**Author(s)**

Layla Parast

## References

Parast, L. & Griffin B.A. (2015). Landmark Estimation of Survival and Treatment Effects in Observational Studies, in press.

Rosenbaum, P. R., & Rubin, D. B. (1983). The central role of the propensity score in observational studies for causal effects. Biometrika, 70(1), 41-55.

Rosenbaum, P. R., & Rubin, D. B. (1984). Reducing bias in observational studies using subclassification on the propensity score. Journal of the American Statistical Association, 79(387), 516-524.

## Examples

```
data(example_obs)
W.weight = ps.wgt.fun(treat = example_obs$treat, cov.for.ps = as.matrix(example_obs$Z))
#executable but takes time
#delta.land.obs(tl=example_obs$TL, dl = example_obs$DL, treat = example_obs$treat, tt=2,
#landmark = 1, short = cbind(example_obs$TS,example_obs$DS), z.cov = as.matrix(example_obs$Z),
#ps.weights = W.weight)
#delta.land.obs(tl=example_obs$TL, dl = example_obs$DL, treat = example_obs$treat, tt=2,
#landmark = 1, short = cbind(example_obs$TS,example_obs$DS), z.cov = as.matrix(example_obs$Z),
#cov.for.ps = as.matrix(example_obs$Z))
```

---

delta.land.rct                *Estimates survival and treatment effect using landmark estimation*

---

## Description

Estimates the probability of survival past some specified time and the treatment effect, defined as the difference in survival at the specified time, using landmark estimation for a randomized trial setting

## Usage

```
delta.land.rct(tl, dl, treat, tt, landmark, short = NULL, z.cov = NULL,
var = FALSE, conf.int = FALSE, weight.perturb = NULL, bw = NULL)
```

## Arguments

| | |
|---|---|
| tl | observed event time of primary outcome, equal to min(T, C) where T is the event time and C is the censoring time. |
| dl | event indicator, equal to I(T<C) where T is the event time and C is the censoring time. |
| treat | treatment indicator, should be 0/1. |
| tt | the time of interest, function estimates the probability of survival past this time |
| landmark | the landmark time |

| short | a matrix of intermediate event information, there should be two columns for each intermediate event, the first column contains the observed intermediate event time, equal to min(TS, C) where TS is the event time and C is the censoring time, and the second column contains the event indicator, equal to I(TS<C) |
|---|---|
| z.cov | matrix of baseline covariate information |
| var | TRUE or FALSE; indicates whether variance estimates for the treatment effect and survival in each group are requested, default is FALSE. |
| conf.int | TRUE or FALSE; indicates whether 95% confidence intervals for the treatment effect and survival in each group are requested, default is FALSE. |
| weight.perturb | a (n1+n0) by x matrix of weights where n1 = length of tl for treatment group 1 and n0 = length of tl for treatment group 0; used for perturbation-resampling, default is null. If var or conf.int is TRUE and weight.perturb is not provided, the function generates exponential(1) weights. |
| bw | bandwidth used for kernel estimation, default is NULL |

**Details**

Let $T_{Li}$ denote the time of the primary event of interest for person $i$, $T_{Si}$ denote the time of the available intermediate event(s), $C_i$ denote the censoring time, $Z_i$ denote the vector of baseline (pretreatment) covariates, and $G_i$ be the treatment group indicator such that $G_i = 1$ indicates treatment and $G_i = 0$ indicates control. Due to censoring, we observe $X_{Li} = min(T_{Li}, C_i)$ and $\delta_{Li} = I(T_{Li} \leq C_i)$ and $X_{Si} = min(T_{Si}, C_i)$ and $\delta_{Si} = I(T_{Si} \leq C_i)$. This function estimates survival at time t within each treatment group, $S_j(t) = P(T_L > t | G = j)$ for $j = 1, 0$ and the treatment effect defined as $\Delta(t) = S_1(t) - S_0(t)$.

To derive these estimates using landmark estimation, we first decompose the quantity into two components $S_j(t) = S_j(t|t_0)S_j(t_0)$ using a landmark time $t_0$ and estimate each component separately. Intermediate event information is used in estimation of the conditional component $S_j(t|t_0)$,

$$S_j(t|t_0) = P(T_L > t | T_L > t_0, G = j) = E[E[I(T_L > t | T_L > t_0, G = j, H)]] = E[S_{j,H}(t|t_0)]$$

where $S_{j,H}(t|t_0) = P(T_L > t | T_L > t_0, G = j, H)$ and $H = \{Z, I(T_S \leq t_0), min(T_S, t_0)\}$. Then $S_{j,H}(t|t_0)$ is estimated in two stages: 1) fitting the Cox proportional hazards model among individuals with $X_L > t_0$ to obtain an estimate of $\beta$, denoted as $\hat{\beta}$,

$$S_{j,H}(t|t_0) = \exp\{-\Lambda_{j,0}(t|t_0)\exp(\beta^T H)\}$$

where $\Lambda_{j,0}(t|t_0)$ is the cumulative baseline hazard in group $j$ and then 2) using a nonparametric kernel Nelson-Aalen estimator to obtain a local constant estimator for the conditional hazard $\Lambda_{j,u}(t|t_0) = -\log[S_{j,u}(t|t_0)]$ as

$$\hat{\Lambda}_{j,u}(t|t_0) = \int_{t_0}^{t} \frac{\sum_i K_h(\hat{U}_i - u)dN_i(z)}{\sum_i K_h(\hat{U}_i - u)Y_i(z)}$$

where $S_{j,u}(t|t_0) = P(T_L > t | T_L > t_0, G = j, \hat{U} = u)$, $\hat{U} = \hat{\beta}^T H$, $Y_i(t) = I(T_L \geq t)$, $N_i(t) = I(T_L \leq t)I(T_L < C)$, $K(\cdot)$ is a smooth symmetric density function, $K_h(x/h)/h$, $h = O(n^{-v})$ is a bandwidth with $1/2 > v > 1/4$, and the summation is over all individuals with $G = j$ and

$X_L > t_0$. The resulting estimate for $S_{j,u}(t|t_0)$ is $\hat{S}_{j,u}(t|t_0) = \exp\{-\hat{\Lambda}_{j,u}(t|t_0)\}$, and the final estimate

$$\hat{S}_j(t|t_0) = \frac{n^{-1}\sum_{i=1}^{n}\hat{S}_j(t|t_0, H_i)I(G_i = 1)I(X_{Li} > t_0)}{n^{-1}\sum_{i=1}^{n}I(G_i = 1)I(X_{Li} > t_0)}$$

is a consistent estimate of $S_j(t|t_0)$.

Estimation of $S_j(t_0)$ uses a similar two-stage approach but using only baseline covariates, to obtain $\hat{S}_j(t_0)$. The final overall estimate of survival at time $t$ is, $\hat{S}_{LM,j}(t) = \hat{S}_j(t|t_0)\hat{S}_j(t_0)$. The treatment effect in terms of the difference in survival at time $t$ is estimated as $\hat{\Delta}_{LM}(t) = \hat{S}_{LM,1}(t) - \hat{S}_{LM,0}(t)$. To obtain an appropriate $h$ we first use the bandwidth selection procedure given by Scott(1992) to obtain $h_{opt}$; and then we let $h = h_{opt}n^{-0.10}$.

To obtain variance estimates and construct confidence intervals, we use a perturbation-resampling method. Specifically, let $\{V^{(b)} = (V_1^{(b)}, ..., V_n^{(b)})^T, b = 1, ...B\}$ be $n \times B$ independent copies of a positive random variable U from a known distribution with unit mean and unit variance such as an Exp(1) distribution. To estimate the variance of our estimates, we appropriately weight the estimates using these perturbation weights to obtain perturbed values: $\hat{S}_{LM,0}(t)^{(b)}$, $\hat{S}_{LM,1}(t)^{(b)}$, and $\hat{\Delta}_{LM}(t)^{(b)}, b = 1, ...B$. We then estimate the variance of each estimate as the empirical variance of the perturbed quantities. To construct confidence intervals, one can either use the empirical percentiles of the perturbed samples or a normal approximation.

## Value

A list is returned:

S.estimate.1    the estimate of survival at the time of interest for treatment group 1, $\hat{S}_1(t) = P(T > t|G = 1)$

S.estimate.0    the estimate of survival at the time of interest for treatment group 0, $\hat{S}_0(t) = P(T > t|G = 0)$

delta.estimate    the estimate of treatment effect at the time of interest

S.var.1    the variance estimate of $\hat{S}_1(t)$; if var = TRUE or conf.int = TRUE

S.var.0    the variance estimate of $\hat{S}_0(t)$; if var = TRUE or conf.int = TRUE

delta.var    the variance estimate of $\hat{\Delta}(t)$; if var = TRUE or conf.int = TRUE

p.value    the p-value from testing $\Delta(t) = 0$; if var = TRUE or conf.int = TRUE

conf.int.normal.S.1
            a vector of size 2; the 95% confidence interval for $\hat{S}_1(t)$ based on a normal approximation; if conf.int = TRUE

conf.int.normal.S.0
            a vector of size 2; the 95% confidence interval for $\hat{S}_0(t)$ based on a normal approximation; if conf.int = TRUE

conf.int.normal.delta
            a vector of size 2; the 95% confidence interval for $\hat{\Delta}(t)$ based on a normal approximation; if conf.int = TRUE

conf.int.quantile.S.1
            a vector of size 2; the 95% confidence interval for $\hat{S}_1(t)$ based on sample quantiles of the perturbed values, described above; if conf.int = TRUE

```
conf.int.quantile.S.0
```
a vector of size 2; the 95% confidence interval for $\hat{S}_0(t)$ based on sample quantiles of the perturbed values, described above; if conf.int = TRUE

```
conf.int.quantile.delta
```
a vector of size 2; the 95% confidence interval for $\hat{\Delta}(t)$ based on sample quantiles of the perturbed values, described above; if conf.int = TRUE

## Author(s)

Layla Parast

## References

Parast, L., Tian, L., & Cai, T. (2014). Landmark Estimation of Survival and Treatment Effect in a Randomized Clinical Trial. Journal of the American Statistical Association, 109(505), 384-394.

Beran, R. (1981). Nonparametric regression with randomly censored survival data. Technical report, University of California Berkeley.

Scott, D. (1992). Multivariate density estimation. Wiley.

## Examples

```
data(example_rct)
#executable but takes time
#delta.land.rct(tl=example_rct$TL, dl = example_rct$DL, treat = example_rct$treat, tt=2,
#landmark = 1, short = cbind(example_rct$TS,example_rct$DS), z.cov = as.matrix(example_rct$Z))
```

---

example_obs                     *Hypothetical data from an observational study*

---

## Description

Hypothetical data from an observational study to be used in examples.

## Usage

```
data(example_obs)
```

## Format

A data frame with 4000 observations on the following 6 variables.

TL  the observed event or censoring time for the primary outcome, equal to min(T, C) where T is the time of the primary outcome and C is the censoring time.

DL  the indicator telling whether the individual was observed to have the event or was censored, equal to 1*(T<C) where T is the time of the primary outcome and C is the censoring time.

TS  the observed event or censoring time for the intermediate event, equal to min(TS, C) where TS is the time of the intermediate event and C is the censoring time.

DS the indicator telling whether the individual was observed to have the intermediate event or was censored, equal to 1*(TS<C) where TS is the time of the primary outcome and C is the censoring time.

Z a baseline covariate vector

treat treatment indicator

## Examples

```
data(example_obs)
names(example_obs)
```

---

example_rct                    *Hypothetical data from a randomized trial*

---

## Description

Hypothetical data from a randomized trial to be used in examples.

## Usage

```
data(example_rct)
```

## Format

A data frame with 3000 observations on the following 6 variables.

TL the observed event or censoring time for the primary outcome, equal to min(T, C) where T is the time of the primary outcome and C is the censoring time.

DL the indicator telling whether the individual was observed to have the event or was censored, equal to 1*(T<C) where T is the time of the primary outcome and C is the censoring time.

TS the observed event or censoring time for the intermediate event, equal to min(TS, C) where TS is the time of the intermediate event and C is the censoring time.

DS the indicator telling whether the individual was observed to have the intermediate event or was censored, equal to 1*(TS<C) where TS is the time of the primary outcome and C is the censoring time.

Z a baseline covariate vector

treat treatment indicator

## Examples

```
data(example_rct)
names(example_rct)
```

---

ps.wgt.fun                      *Calculates propensity score weights*

---

**Description**

Calculates propensity score (or inverse probability of treatment) weights given the treatment indicator and available baseline (pretreatment) covariates.

**Usage**

```
ps.wgt.fun(treat, cov.for.ps, weight = NULL)
```

**Arguments**

treat           treatment indicator, should be 0/1.

cov.for.ps      matrix of covariates to be used to estimate propensity score (or inverse probability of treatment) weights

weight          a (n1+n0) by x matrix of weights where n1 = number of observations in treatment group 1 and n0 = number of observations in treatment group 0; used for perturbation-resampling, default is null.

**Details**

Let $Z_i$ denote the matrix of baseline (pretreatment) covariates and $G_i$ be the treatment group indicator such that $G_i = 1$ indicates treatment and $G_i = 0$ indicates control. This function estimates $P = P(G_i = 1|Z_i)$ using logistic regression. The propensity score (or inverse probability of treatment) weights are then equal to $1/\hat{P}$ for those in treatment group 1 and $1/(1 - \hat{P})$ for those in treatment group 0. These weights reflect the situation where the average treatment effect (ATE) is of interest, not average treatment effect in the treated (ATT).

**Value**

propensity score (or inverse probability of treatment) weights

**Author(s)**

Layla Parast

**References**

Rosenbaum, P. R., & Rubin, D. B. (1983). The central role of the propensity score in observational studies for causal effects. Biometrika, 70(1), 41-55.

Rosenbaum, P. R., & Rubin, D. B. (1984). Reducing bias in observational studies using subclassification on the propensity score. Journal of the American Statistical Association, 79(387), 516-524.

## Examples

```
data(example_obs)
W.weight = ps.wgt.fun(treat = example_obs$treat, cov.for.ps = as.matrix(example_obs$Z))
delta.iptw.km(tl=example_obs$TL, dl = example_obs$DL, treat = example_obs$treat, tt=2,
ps.weights = W.weight)
```

---

| surv.iptw.km | *Estimates survival using inverse probability of treatment weighted (IPTW) Kaplan-Meier estimation* |
|---|---|

---

## Description

Estimates the probability of survival past some specified time using inverse probability of treatment weighted (IPTW) Kaplan-Meier estimation

## Usage

```
surv.iptw.km(tl, dl, tt, var = FALSE, conf.int = FALSE, ps.weights,
weight.perturb = NULL,perturb.ps = FALSE, perturb.vector = FALSE)
```

## Arguments

| | |
|---|---|
| tl | observed event time of primary outcome, equal to min(T, C) where T is the event time and C is the censoring time. |
| dl | event indicator, equal to I(T<C) where T is the event time and C is the censoring time. |
| tt | the time of interest, function estimates the probability of survival past this time |
| var | TRUE or FALSE; indicates whether a variance estimate for survival is requested, default is FALSE. |
| conf.int | TRUE or FALSE; indicates whether a 95% confidence interval for survival is requested, default is FALSE. |
| ps.weights | propensity score (or inverse probability of treatment) weights |
| weight.perturb | a n by x matrix of weights where n = length of tl; used for perturbation-resampling, default is null. If var or conf.int is TRUE and weight.perturb is not provided, the function generates exponential(1) weights. |
| perturb.ps | TRUE or FALSE indicating whether the weight.perturb matrix includes the perturbed propensity score (or inverse probability of treatment) weights |
| perturb.vector | TRUE or FALSE; indicates whether a vector of the perturbed values of the survival estimate is requested, default is FALSE. This argument is ignored if both var and conf.int are FALSE. |

## Details

See documentation for delta.iptw.km for details.

## Value

A list is returned:

| | |
|---|---|
| S.estimate | the estimate of survival at the time of interest, $\hat{S}(t) = P(T > t)$ |
| S.var | the variance estimate of $\hat{S}(t)$; if var = TRUE or conf.int = TRUE |
| conf.int.normal.S | |
| | a vector of size 2; the 95% confidence interval for $\hat{S}(t)$ based on a normal approximation; if conf.int = TRUE |
| conf.int.quantile.S | |
| | a vector of size 2; the 95% confidence interval for $\hat{S}(t)$ based on sample quantiles of the perturbed values, described above; if conf.int = TRUE |
| perturb.vector | a vector of size x where x is the number of columns of the provided weight.perturb matrix (or x=500 if weight.perturb is not provided); the perturbed values of $\hat{S}(t)$; if perturb.vector = TRUE and either var=TRUE or conf.int = TRUE |

## Author(s)

Layla Parast

## References

Xie, J., & Liu, C. (2005). Adjusted Kaplan-Meier estimator and log-rank test with inverse probability of treatment weighting for survival data. Statistics in Medicine, 24(20), 3089-3110.

## Examples

```
data(example_obs)
W.weight = ps.wgt.fun(treat = example_obs$treat, cov.for.ps = as.matrix(example_obs$Z))
example_obs.treat = example_obs[example_obs$treat == 1,]
surv.iptw.km(tl=example_obs.treat$TL, dl = example_obs.treat$DL, tt=2, ps.weights =
W.weight[example_obs$treat == 1])
```

---

surv.km                                    *Estimates survival using Kaplan-Meier estimation*

---

## Description

Estimates the probability of survival past some specified time using Kaplan-Meier estimation

## Usage

```
surv.km(tl, dl, tt, var = FALSE, conf.int = FALSE, weight.perturb = NULL,
perturb.vector = FALSE)
```

5*surv.km* 19

## Arguments

| | |
|---|---|
| `tl` | observed event time of primary outcome, equal to min(T, C) where T is the event time and C is the censoring time. |
| `dl` | event indicator, equal to I(T<C) where T is the event time and C is the censoring time. |
| `tt` | the time of interest, function estimates the probability of survival past this time |
| `var` | TRUE or FALSE; indicates whether a variance estimate for survival is requested, default is FALSE. |
| `conf.int` | TRUE or FALSE; indicates whether a 95% confidence interval for survival is requested, default is FALSE. |
| `weight.perturb` | a n by x matrix of weights where n = length of tl; used for perturbation-resampling, default is null. If var or conf.int is TRUE and weight.perturb is not provided, the function generates exponential(1) weights. |
| `perturb.vector` | TRUE or FALSE; indicates whether a vector of the perturbed values of the survival estimate is requested, default is FALSE. This argument is ignored if both var and conf.int are FALSE. |

## Details

See documentation for delta.km for details.

## Value

A list is returned:

| | |
|---|---|
| `S.estimate` | the estimate of survival at the time of interest, $\hat{S}(t) = P(T > t)$ |
| `S.var` | the variance estimate of $\hat{S}(t)$; if var = TRUE or conf.int = TRUE |
| `conf.int.normal.S` | a vector of size 2; the 95% confidence interval for $\hat{S}(t)$ based on a normal approximation; if conf.int = TRUE |
| `conf.int.quantile.S` | a vector of size 2; the 95% confidence interval for $\hat{S}(t)$ based on sample quantiles of the perturbed values, described above; if conf.int = TRUE |
| `perturb.vector` | a vector of size x where x is the number of columns of the provided weight.perturb matrix (or x=500 if weight.perturb is not provided); the perturbed values of $\hat{S}(t)$; if perturb.vector = TRUE and either var=TRUE or conf.int = TRUE |

## Author(s)

Layla Parast

## References

Kaplan, E. L., & Meier, P. (1958). Nonparametric estimation from incomplete observations. Journal of the American Statistical Association, 53(282), 457-481.

## Examples

```
data(example_rct)
example_rct.treat = example_rct[example_rct$treat == 1,]
surv.km(tl=example_rct.treat$TL, dl = example_rct.treat$DL, tt=2)
```

---

surv.land.obs                *Estimates survival using landmark estimation*

---

## Description

Estimates the probability of survival past some specified time using landmark estimation for an observational study setting

## Usage

```
surv.land.obs(tl, dl, tt, landmark, short = NULL, z.cov = NULL, var = FALSE,
conf.int = FALSE, ps.weights, weight.perturb = NULL, perturb.ps = FALSE,
perturb.vector = FALSE, bw = NULL)
```

## Arguments

| | |
|---|---|
| tl | observed event time of primary outcome, equal to min(T, C) where T is the event time and C is the censoring time. |
| dl | event indicator, equal to I(T<C) where T is the event time and C is the censoring time. |
| tt | the time of interest, function estimates the probability of survival past this time |
| landmark | the landmark time |
| short | a matrix of intermediate event information, there should be two columns for each intermediate event, the first column contains the observed intermediate event time, equal to min(TS, C) where TS is the event time and C is the censoring time, and the second column contains the event indicator, equal to I(TS<C) |
| z.cov | matrix of baseline covariate information |
| var | TRUE or FALSE; indicates whether a variance estimate for survival is requested, default is FALSE. |
| conf.int | TRUE or FALSE; indicates whether a 95% confidence interval for survival is requested, default is FALSE. |
| ps.weights | propensity score (or inverse probability of treatment) weights |
| weight.perturb | a n by x matrix of weights where n = length of tl; used for perturbation-resampling, default is null. If var or conf.int is TRUE and weight.perturb is not provided, the function generates exponential(1) weights. |
| perturb.ps | TRUE or FALSE indicating whether the weight.perturb matrix includes the perturbed propensity score (or inverse probability of treatment) weights |
| perturb.vector | TRUE or FALSE; indicates whether a vector of the perturbed values of the survival estimate is requested, default is FALSE. This argument is ignored if both var and conf.int are FALSE. |
| bw | bandwidth used for kernel estimation, default is NULL |

**Details**

See documentation for delta.land.obs for details.

**Value**

A list is returned:

| | |
|---|---|
| `S.estimate` | the estimate of survival at the time of interest, $\hat{S}(t) = P(T > t)$ |
| `S.var` | the variance estimate of $\hat{S}(t)$; if var = TRUE or conf.int = TRUE |
| `conf.int.normal.S` | |
| | a vector of size 2; the 95% confidence interval for $\hat{S}(t)$ based on a normal approximation; if conf.int = TRUE |
| `conf.int.quantile.S` | |
| | a vector of size 2; the 95% confidence interval for $\hat{S}(t)$ based on sample quantiles of the perturbed values, described above; if conf.int = TRUE |
| `perturb.vector` | a vector of size x where x is the number of columns of the provided weight.perturb matrix (or x=500 if weight.perturb is not provided); the perturbed values of $\hat{S}(t)$; if perturb.vector = TRUE and either var=TRUE or conf.int = TRUE |

**Author(s)**

Layla Parast

**References**

Parast, L. & Griffin B.A. (2015). Landmark Estimation of Survival and Treatment Effects in Observational Studies, in press.

**Examples**

```
data(example_obs)
W.weight = ps.wgt.fun(treat = example_obs$treat, cov.for.ps = as.matrix(example_obs$Z))
example_obs.treat = example_obs[example_obs$treat == 1,]
#executable but takes time
#surv.land.obs(tl=example_obs.treat$TL, dl = example_obs.treat$DL, tt=2, landmark = 1,
#short = cbind(example_obs.treat$TS,example_obs.treat$DS), z.cov = example_obs.treat$Z,
#ps.weights = W.weight[example_obs$treat == 1])
```

---

surv.land.rct          *Estimates survival using landmark estimation*

---

**Description**

Estimates the probability of survival past some specified time using landmark estimation for a randomized trial setting

**Usage**

```
surv.land.rct(tl, dl, tt, landmark, short = NULL, z.cov = NULL, var = FALSE,
conf.int = FALSE, weight.perturb = NULL, perturb.vector = FALSE, bw = NULL)
```

**Arguments**

| | |
|---|---|
| tl | observed event time of primary outcome, equal to min(T, C) where T is the event time and C is the censoring time. |
| dl | event indicator, equal to I(T<C) where T is the event time and C is the censoring time. |
| tt | the time of interest, function estimates the probability of survival past this time |
| landmark | the landmark time |
| short | a matrix of intermediate event information, there should be two columns for each intermediate event, the first column contains the observed intermediate event time, equal to min(TS, C) where TS is the event time and C is the censoring time, and the second column contains the event indicator, equal to I(TS<C) |
| z.cov | matrix of baseline covariate information |
| var | TRUE or FALSE; indicates whether a variance estimate for survival is requested, default is FALSE. |
| conf.int | TRUE or FALSE; indicates whether a 95% confidence interval for survival is requested, default is FALSE. |
| weight.perturb | a n by x matrix of weights where n = length of tl; used for perturbation-resampling, default is null. If var or conf.int is TRUE and weight.perturb is not provided, the function generates exponential(1) weights. |
| perturb.vector | TRUE or FALSE; indicates whether a vector of the perturbed values of the survival estimate is requested, default is FALSE. This argument is ignored if both var and conf.int are FALSE. |
| bw | bandwidth used for kernel estimation, default is NULL |

**Details**

See documentation for delta.land.rct for details.

**Value**

A list is returned:

| | |
|---|---|
| S.estimate | the estimate of survival at the time of interest, $\hat{S}(t) = P(T > t)$ |
| S.var | the variance estimate of $\hat{S}(t)$; if var = TRUE or conf.int = TRUE |
| conf.int.normal.S | |
| | a vector of size 2; the 95% confidence interval for $\hat{S}(t)$ based on a normal approximation; if conf.int = TRUE |
| conf.int.quantile.S | |
| | a vector of size 2; the 95% confidence interval for $\hat{S}(t)$ based on sample quantiles of the perturbed values, described above; if conf.int = TRUE |

perturb.vector  a vector of size x where x is the number of columns of the provided weight.perturb matrix (or x=500 if weight.perturb is not provided); the perturbed values of $\hat{S}(t)$; if perturb.vector = TRUE and either var=TRUE or conf.int = TRUE

## Author(s)

Layla Parast

## References

Parast, L., Tian, L., & Cai, T. (2014). Landmark Estimation of Survival and Treatment Effect in a Randomized Clinical Trial. Journal of the American Statistical Association, 109(505), 384-394.

## Examples

```
data(example_rct)
example_rct.treat = example_rct[example_rct$treat == 1,]
#executable but takes time
#surv.land.rct(tl=example_rct.treat$TL, dl = example_rct.treat$DL, tt=2, landmark = 1,
#short = cbind(example_rct.treat$TS,example_rct.treat$DS), z.cov = example_rct.treat$Z)
```

# Index