# Package 'survivalsurrogate'

June 5, 2025

Type Package

Title Evaluate a Longitudinal Surrogate with a Censored Outcome
Version 1.1
<b>Date</b> 2025-06-05
Provides influence function-based methods to evaluate a longitudinal surrogate marker in a censored time-to-event outcome setting, with plug-in and targeted maximum likelihood estimation options. Details are described in: Agniel D and Parast L (2025). ``Robust Evaluation of Longitudinal Surrogate Markers with Censored Data." Journal of the Royal Statistical Society: Series B <doi:10.1093 jrsssb="" qkae119="">. A tutorial for this package can be found at <https: survivalsurrogate="" www.laylaparast.com=""> and a Shiny App implementing the package can be found at <https: parastlab.shinyapps.io="" survivalsurrogateapp=""></https:>.</https:></doi:10.1093>
License GPL
Imports stats, dplyr, magrittr, glue, mlr3, purrr, SparseM, rBeta2009, data.table, utils, rpart
Suggests mlr3learners
NeedsCompilation no
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Maintainer Layla Parast <pre><pre></pre></pre>
<b>Depends</b> R (>= 3.5.0)
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_ 11 3 3 1	estimate_R	Estimates the proportion of the treatment effect explained
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# Description

Estimates the proportion of the treatment effect on the censored primary outcome that is explained by the longitudinal surrogate marker, given the estimated influence functions for the overall treatment effect (delta) and the residual treatment effect (delta\_s).

# Usage

```
estimate_R(delta_if, delta_s_if, delta = NULL, delta_s = NULL, se_type = "asymptotic",
n_boot = NULL, alpha = 0.05)
```

## **Arguments**

delta_if	Influence function estimates for delta.
delta_s_if	Influence function estimates for delta_s.
delta	(Optional) Defaults to the mean of the delta influence function estimates.
delta_s	(Optional) Defaults to the mean of the delta_s influence function estimates.
se_type	Type of standard error estimation, choices are "asymptotic" or "bootstrap".
n_boot	(Optional unless se_type = "bootstrap") Number of boostrap samples.
alpha	(Optional) Alpha level used for confidence interval. If not provided, this is set to 0.05.

## Value

A dataframe with the following components:

estimand	Indicates what estimand is estimated, including the treatment effect (delta), residual treatment effect (delta.s), and proportion of treatment effect explained (R) by the longitudinal surrogate marker.
estimate	Estimates of the treatment effect (delta), residual treatment effect (delta.s), and proportion of treatment effect explained (R) by the longitudinal surrogate marker.
se	Estimated standard errors.
ci_l	Lower bound of the confidence intervals.
ci_h	Upper bound of the confidence intervals.

# References

Agniel D and Parast L (2025). "Robust Evaluation of Longitudinal Surrogate Markers with Censored Data." Journal of the Royal Statistical Society: Series B; doi:10.1093/jrsssb/qkae119.

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## **Examples**

```
data(exampledata)
names(exampledata)
library(glue)
library(rpart)
library(mlr3)
library(dplyr)
library(mlr3learners)
tt <- 5
t0 <- 4
yvars <- paste0('Y_-', 0:tt)
lrnc <- glue('regr.rpart')</pre>
lrnb <- glue('classif.log_reg')</pre>
p_deltahat <- plugin_delta(</pre>
    data = exampledata,
    folds = 'ff',
    id = 'ID',
    x = 'X_0',
    g = 'G_0',
    a = paste0('A_', 0:tt),
    y = yvars,
    s = paste0('S_', 0:t0),
    binary_lrnr = lrn(lrnb, predict_type = 'prob'),
    cont_lrnr = lrn(lrnc),
    truncate_e = 0.005,
    verbose = FALSE
  )
p_deltahat_s <- plugin_delta_s(</pre>
    data = exampledata,
    folds = 'ff',
    id = 'ID',
    x = 'X_0',
    g = 'G_0',
    a = paste0('A_', 0:tt),
    y = yvars,
    s = paste0('S_', 0:t0),
    binary_lrnr = lrn(lrnb, predict_type = 'prob'),
    cont_lrnr = lrn(lrnc),
    t0=t0,
    truncate_pi = 0.005,
    truncate_e = 0.005,
    verbose = FALSE
estimate_R(p_deltahat$if_data[[1]]$eif,
p_deltahat_s$if_data[[1]]$eif)
```

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## **Description**

Example dataset with longitudinal surrogate marker and censored primary outcome

## Usage

```
data("exampledata")
```

#### **Format**

A data frame with 1000 observations on the following 21 variables. Here, the landmark time is 4 and the final time point is 5. The surrogate is measured at the following time points: 0,1,2,3,4.

- ID Unique individual ID
- X\_0 Baseline covariate vector.
- G\_0 Treatment indicator vector.
- Y\_0 Primary outcome variable at time 0.
- S\_0 Surrogate marker value at time 0.
- Y\_1 Primary outcome variable at time 1.
- S\_1 Surrogate marker value at time 1.
- Y\_2 Primary outcome variable at time 2.
- S\_2 Surrogate marker value at time 2.
- Y\_3 Primary outcome variable at time 3.
- S\_3 Surrogate marker value at time 3.
- Y\_4 Primary outcome variable at time 4.
- S\_4 Surrogate marker value at time 4.
- Y\_5 Primary outcome variable at time 5.
- ff Fold number.
- A\_0 Observation variable at time 0.
- A\_1 Observation variable at time 1.
- A\_2 Observation variable at time 2.
- A\_3 Observation variable at time 3.
- A\_4 Observation variable at time 4.
- A\_5 Observation variable at time 5.

plugin\_delta

Treatment effect estimation using plug-in estimator

# Description

Estimates the treatment effect using the plug-in estimator.

## Usage

plugin\_delta 5

## **Arguments**

data

A dataframe containing all necessary variables for estimation. The functions in this package require the dataframe to be in a specific form. Therefore, you will need to reformat your dataset as follows. At a minimum, you will need variables in your dataframe that indicate (1) the folds for crossfitting; (2) a unique observation identifier; (3) baseline covariates, if there are none you must have a variable with all values equal to 1 to provide to the argument x below; (4) a variable indicating treatment group which should be 1 for treatment and 0 for control; (5) a set of variables that contain the surrogate marker value at each time point up to and including the landmark time, denoted t0; (6) a set of variables that indicate primary outcome status at each time point where the surrogate marker is measured, in addition to measurements beyond t0 up to a final time point t > t0. Optionally, if there is censoring, you may also include a set of variables that indicate observation status (1 if not censored, 0 if censored) at all time points. See the exampledata for an example where t0=4 and t=5.

folds A vector defining crossfitting folds for nuisance estimation.

A string giving the name of the column with unique unit IDs (e.g., individual

A character vector of covariate names to adjust for in nuisance estimation. At a Х

minimum this must have one covariate equal to 1 for all individuals.

A string indicating the column name of the treatment indicator with 1 for treat-

ment and 0 for control.

(Optional) A character vector of the column names indicating observation status at each time point. Specifically,  $A_t = 1$  if the individual is still under observation (i.e., uncensored) at time t, meaning their outcome status could in principle be measured at that time. A value of 0 means the individual was censored prior

to t. If not provided, assumed to be 1 for all time points.

A character vector of the column names indicating primary outcome status at each time point. Specifically,  $Y_t = 1$  if the primary event (e.g., failure, relapse, death) has not yet occurred by time t, and the individual is still at risk. A value

of 0 means the primary event occurred on or before time t.

A character vector of the column names indicating the surrogate marker values measured at each time point, where the value is NA if the individual is no longer observable at that time point.

Learner object or specification used for estimating binary nuisance components

(e.g., propensity scores, censoring).

cont\_lrnr Learner object used for estimating continuous-valued regressions.

(Optional) Column name of propensity score estimates. If not provided, these

will be estimated.

(Optional) Vector of column names for censoring probabilities under treatment. gamma1

If not provided, these will be estimated.

(Optional) Vector of column names for censoring probabilities under control. If gamma0

not provided, these will be estimated.

(Optional) Names of estimated hazards under treatment. If not provided, these mu1

will be estimated.

mu0 (Optional) Names of estimated hazards under control. If not provided, these will

be estimated.

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binary\_lrnr

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Q1	(Optional) Names of estimated conditional means under treatment. If not provided, these will be estimated.
Q0	(Optional) Names of estimated conditional means under control. If not provided, these will be estimated.
truncate_e	Numeric truncation level for propensity scores to avoid division by near-zero values. Default is 1e-12.
verbose	Logical; if TRUE, print progress messages.

## Value

A dataframe with the following components:

plugin\_est Plug-in estimate of the treatment effect

plugin\_se Estimated standard error of the plug-in estimator, based on the influence function.

if\_data A nested data frame containing the influence function contributions for each observation.

## References

Agniel D and Parast L (2025). "Robust Evaluation of Longitudinal Surrogate Markers with Censored Data." Journal of the Royal Statistical Society: Series B; doi:10.1093/jrsssb/qkae119.

## **Examples**

```
data(exampledata)
names(exampledata)
library(glue)
library(rpart)
library(mlr3)
library(dplyr)
library(mlr3learners)
tt <- 5
t0 <- 4
yvars <- paste0('Y_', 0:tt)</pre>
lrnc <- glue('regr.rpart')</pre>
lrnb <- glue('classif.log_reg')</pre>
p_deltahat <- plugin_delta(</pre>
    data = exampledata,
    folds = 'ff',
    id = 'ID',
    x = 'X_0'
    g = 'G_0',
    a = paste0('A_', 0:tt),
    y = yvars,
    s = paste0('S_', 0:t0),
    binary_lrnr = lrn(lrnb, predict_type = 'prob'),
    cont_lrnr = lrn(lrnc),
    truncate_e = 0.005,
    verbose = FALSE
p_deltahat
```

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plugin\_delta\_s

Residual treatment effect estimation using the plug-in estimator

#### **Description**

Estimates the residual treatment effect using the plug-in estimator for evaluating a longitudinal surrogate marker.

## Usage

```
plugin_delta_s(data, folds, id, x, g, a = NULL, y, s, binary_lrnr = NULL, cont_lrnr
= NULL, t0 = length(s), e = NULL, gamma1 = NULL, gamma0 = NULL, mu1 = NULL, mu0 = NULL,
pi = NULL, pistar = NULL, Q1 = NULL, Q0 = NULL, truncate_e = 1e-12, truncate_pi = 1e-12,
se_type = "asymptotic", n_boot = NULL, alpha = 0.05, verbose = FALSE, retain_data
= FALSE)
```

## **Arguments**

data

A dataframe containing all necessary variables for estimation. The functions in this package require the dataframe to be in a specific form. Therefore, you will need to reformat your dataset as follows. At a minimum, you will need variables in your dataframe that indicate (1) the folds for crossfitting; (2) a unique observation identifier; (3) baseline covariates, if there are none you must have a variable with all values equal to 1 to provide to the argument x below; (4) a variable indicating treatment group which should be 1 for treatment and 0 for control; (5) a set of variables that contain the surrogate marker value at each time point up to and including the landmark time, denoted t0; (6) a set of variables that indicate primary outcome status at each time point where the surrogate marker is measured, in addition to measurements beyond t0 up to a final time point t > t0. Optionally, if there is censoring, you may also include a set of variables that indicate observation status (1 if not censored, 0 if censored) at all time points. See the exampledata for an example where t0=4 and t=5.

folds

A vector defining crossfitting folds for nuisance estimation.

id

A string giving the name of the column with unique unit IDs (e.g., individual ID).

(

A character vector of covariate names to adjust for in nuisance estimation. At a minimum this must have one covariate equal to 1 for all individuals.

g

A string indicating the column name of the treatment indicator with 1 for treatment and 0 for control.

а

(Optional) A character vector of the column names indicating observation status at each time point. Specifically,  $A_t = 1$  if the individual is still under observation (i.e., uncensored) at time t, meaning their outcome status could in principle be measured at that time. A value of 0 means the individual was censored prior to t. If not provided, assumed to be 1 for all time points.

У

A character vector of the column names indicating primary outcome status at each time point. Specifically,  $Y_t = 1$  if the primary event (e.g., failure, relapse, death) has not yet occurred by time t, and the individual is still at risk. A value of 0 means the primary event occurred on or before time t.

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s A character vector of the column names indicating the surrogate marker values measured at each time point, where the value is NA if the individual is no longer observable at that time point. binary\_lrnr Learner object or specification used for estimating binary nuisance components (e.g., propensity scores, censoring). cont\_lrnr Learner object used for estimating continuous-valued outcome regressions. t0 Landmark time after which the surrogate is not observed. (Optional) Column name of propensity score estimates. If not provided, these e will be estimated. (Optional) Vector of column names for censoring probabilities under treatment. gamma1 If not provided, these will be estimated. gamma0 (Optional) Vector of column names for censoring probabilities under control. If not provided, these will be estimated. (Optional) Names of estimated hazards under treatment. If not provided, these mu1 will be estimated. (Optional) Names of estimated hazards under control. If not provided, these will mu0 be estimated. (Optional) Vector of column names giving estimated 'propensity score' for treatрi ment conditional on future values of the surrogate up to time k. See Agniel and Parast (2025+) for full definition. If not provided, these will be estimated. pistar (Optional) Vector of column names giving estimated 'propensity score' for treatment conditional on future values of the surrogate up to time k-1. See Agniel and Parast (2025+) for full definition. If not provided, these will be estimated. Q1 (Optional) Names of estimated conditional means under treatment. If not provided, these will be estimated. 00 (Optional) Names of estimated conditional means under control. If not provided, these will be estimated. Numeric truncation level for propensity scores to avoid division by near-zero truncate e values. Default is 1e-12. Truncation threshold for surrogate-conditional propensity scores to avoid instatruncate\_pi bility. Default is 1e-12. Type of standard error estimation, choices are "asymptotic" or "bootstrap". se\_type n\_boot (Optional unless se type = "bootstrap") Number of boostrap samples. alpha Significance level for confidence intervals. Default is 0.05. verbose Logical; if TRUE, print progress messages. retain\_data Logical; if TRUE, retains full dataset with estimated components in the output.

## Value

A dataframe with the following components:

plugin\_est The plug-in estimate of the residual treatment effect at the landmark time.

plugin\_se Standard error of the estimate, based on influence function or bootstrap.

ci\_l Lower bound of the confidence interval.

ci\_h Upper bound of the confidence interval.

if\_data A list containing the dataset with the efficient influence function if retain\_data = TRUE.

#### References

Agniel D and Parast L (2025). "Robust Evaluation of Longitudinal Surrogate Markers with Censored Data." Journal of the Royal Statistical Society: Series B; doi:10.1093/jrsssb/qkae119.

## **Examples**

```
data(exampledata)
names(exampledata)
library(glue)
library(rpart)
library(mlr3)
library(dplyr)
library(mlr3learners)
tt <- 5
t0 <- 4
yvars <- paste0('Y_', 0:tt)</pre>
lrnc <- glue('regr.rpart')</pre>
lrnb <- glue('classif.log_reg')</pre>
p_deltahat_s <- plugin_delta_s(</pre>
    data = exampledata,
    folds = 'ff',
    id = 'ID',
    x = 'X_0'
    g = 'G_0',
    a = paste0('A_', 0:tt),
    y = yvars,
    s = paste0('S_', 0:t0),
    binary_lrnr = lrn(lrnb, predict_type = 'prob'),
    cont_lrnr = lrn(lrnc),
    t0=t0,
    truncate_pi = 0.005,
    truncate_e = 0.005,
    verbose = FALSE
p_deltahat_s
```

tmle\_delta

Treatment effect estimation using TMLE

# Description

Estimates the treatment effect using targeted maximum likelihood estimation (TMLE).

# Usage

```
tmle_delta(data, folds, id, x, g, a = NULL, y, s, binary_lrnr = NULL, cont_lrnr = NULL, e = NULL, gamma1 = NULL, gamma0 = NULL, truncate_e = 1e-12, verbose = FALSE)
```

## **Arguments**

data

A dataframe containing all necessary variables for estimation. The functions in this package require the dataframe to be in a specific form. Therefore, you will need to reformat your dataset as follows. At a minimum, you will need variables in your dataframe that indicate (1) the folds for crossfitting; (2) a unique observation identifier; (3) baseline covariates, if there are none you must have a variable with all values equal to 1 to provide to the argument x below; (4) a variable indicating treatment group which should be 1 for treatment and 0 for control; (5) a set of variables that contain the surrogate marker value at each time point up to and including the landmark time, denoted t0; (6) a set of variables that indicate primary outcome status at each time point where the surrogate marker is measured, in addition to measurements beyond t0 up to a final time point t > t0. Optionally, if there is censoring, you may also include a set of variables that indicate observation status (1 if not censored, 0 if censored) at all time points. See the exampledata for an example where t0=4 and t=5.

folds A vector defining crossfitting folds for nuisance estimation.

id A string giving the name of the column with unique unit IDs (e.g., individual

A character vector of covariate names to adjust for in nuisance estimation. At a Х

minimum this must have one covariate equal to 1 for all individuals.

A string indicating the column name of the treatment indicator with 1 for treat-

ment and 0 for control.

(Optional) A character vector of the column names indicating observation status at each time point. Specifically,  $A_t = 1$  if the individual is still under observation (i.e., uncensored) at time t, meaning their outcome status could in principle be measured at that time. A value of 0 means the individual was censored prior

to t. If not provided, assumed to be 1 for all time points.

A character vector of the column names indicating primary outcome status at each time point. Specifically,  $Y_t = 1$  if the primary event (e.g., failure, relapse, death) has not yet occurred by time t, and the individual is still at risk. A value

of 0 means the primary event occurred on or before time t.

A character vector of the column names indicating the surrogate marker values measured at each time point, where the value is NA if the individual is no longer

observable at that time point.

binary\_lrnr Learner object or specification used for estimating binary nuisance components

(e.g., propensity scores, censoring).

Learner object used for estimating continuous-valued outcome regressions. cont\_lrnr

(Optional) Column name of propensity score estimates. If not provided, these

will be estimated.

gamma1 (Optional) Vector of column names for censoring probabilities under treatment.

If not provided, these will be estimated.

gamma0 (Optional) Vector of column names for censoring probabilities under control. If

not provided, these will be estimated.

truncate\_e Numeric truncation level for propensity scores to avoid division by near-zero

values. Default is 1e-12.

verbose Logical; if TRUE, print progress messages.

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#### Value

A dataframe with the following components:

tmle\_est TMLE estimate of the treatment effect.

tmle\_se Estimated standard error of the TMLE estimator, based on the influence function.

if\_data A nested data frame containing the influence function contributions for each observation.

#### References

Agniel D and Parast L (2025). "Robust Evaluation of Longitudinal Surrogate Markers with Censored Data." Journal of the Royal Statistical Society: Series B; doi:10.1093/jrsssb/qkae119.

## **Examples**

```
data(exampledata)
names(exampledata)
library(glue)
library(rpart)
library(mlr3)
library(dplyr)
library(mlr3learners)
tt <- 5
t0 <- 4
yvars <- paste0('Y_', 0:tt)</pre>
lrnc <- glue('regr.rpart')</pre>
lrnb <- glue('classif.log_reg')</pre>
tml_deltahat <- tmle_delta(data = exampledata,</pre>
                               folds = 'ff',
                               id = 'ID',
                               x = 'X_0',
                               g = 'G_0'
                               a = paste0('A_', 0:tt),
                               y = yvars,
                               s = paste0('S_', 0:t0),
                               binary_lrnr = lrn(lrnb, predict_type = 'prob'),
                               cont_lrnr = lrn(lrnc),
                               truncate_e = 0.005,
                               verbose = FALSE)
tml_deltahat
```

tmle\_delta\_s

Residual treatment effect estimation using TMLE

## **Description**

Estimates the residual treatment effect using targeted maximum likelihood estimation (TMLE) for evaluating a longitudinal surrogate marker.

#### Usage

```
tmle_delta_s(data, folds, id, x, g, a = NULL, y, s, binary_lrnr = NULL, cont_lrnr
= NULL, t0 = length(s), e = NULL, gamma1 = NULL, gamma0 = NULL, pi = NULL,
pistar = NULL, truncate_e = 1e-12, verbose = FALSE, retain_data = FALSE)
```

#### **Arguments**

data

A dataframe containing all necessary variables for estimation. The functions in this package require the dataframe to be in a specific form. Therefore, you will need to reformat your dataset as follows. At a minimum, you will need variables in your dataframe that indicate (1) the folds for crossfitting; (2) a unique observation identifier; (3) baseline covariates, if there are none you must have a variable with all values equal to 1 to provide to the argument x below; (4) a variable indicating treatment group which should be 1 for treatment and 0 for control; (5) a set of variables that contain the surrogate marker value at each time point up to and including the landmark time, denoted t0; (6) a set of variables that indicate primary outcome status at each time point where the surrogate marker is measured, in addition to measurements beyond t0 up to a final time point t > t0. Optionally, if there is censoring, you may also include a set of variables that indicate observation status (1 if not censored, 0 if censored) at all time points. See the exampledata for an example where t0=4 and t=5.

folds

A vector defining crossfitting folds for nuisance estimation.

id

A string giving the name of the column with unique unit IDs (e.g., individual ID)

A character vector of covariate names to adjust for in nuisance estimation. At a minimum this must have one covariate equal to 1 for all individuals.

g

Х

A string indicating the column name of the treatment indicator with 1 for treatment and 0 for control.

а

(Optional) A character vector of the column names indicating observation status at each time point. Specifically,  $A_t = 1$  if the individual is still under observation (i.e., uncensored) at time t, meaning their outcome status could in principle be measured at that time. A value of 0 means the individual was censored prior to t. If not provided, assumed to be 1 for all time points.

У

A character vector of the column names indicating primary outcome status at each time point. Specifically,  $Y_t = 1$  if the primary event (e.g., failure, relapse, death) has not yet occurred by time t, and the individual is still at risk. A value of 0 means the primary event occurred on or before time t.

S

A character vector of the column names indicating the surrogate marker values measured at each time point, where the value is NA if the individual is no longer observable at that time point.

binary\_lrnr

Learner object or specification used for estimating binary nuisance components (e.g., propensity scores, censoring).

cont\_lrnr

Learner object used for estimating continuous-valued outcome regressions.

t0

Landmark time after which the surrogate is not observed.

e

(Optional) Column name of propensity score estimates. If not provided, these will be estimated.

gamma1

(Optional) Vector of column names for censoring probabilities under treatment. If not provided, these will be estimated.

S

\_

gamma0	(Optional) Vector of column names for censoring probabilities under control. If not provided, these will be estimated.
pi	(Optional) Vector of column names giving estimated 'propensity score' for treatment conditional on future values of the surrogate up to time k. See Agniel and Parast (2025+) for full definition. If not provided, these will be estimated.
pistar	(Optional) Vector of column names giving estimated 'propensity score' for treatment conditional on future values of the surrogate up to time k-1. See Agniel and Parast (2025+) for full definition. If not provided, these will be estimated.
truncate_e	Numeric truncation level for propensity scores to avoid division by near-zero values. Default is 1e-12.
verbose	Logical; if TRUE, print progress messages.
retain_data	Logical; if TRUE, the function return the full data and influence function values.

#### Value

A dataframe with the following components:

tmle_est	TMLE estimate of the residual treatment effect.
tmle_se	Estimated standard error using the empirical standard deviation of the influence function.
if_data	(Optional) Full dataset joined with estimated influence function contributions.

## References

Agniel D and Parast L (2025). "Robust Evaluation of Longitudinal Surrogate Markers with Censored Data." Journal of the Royal Statistical Society: Series B; doi:10.1093/jrsssb/qkae119.

# **Examples**

```
data(exampledata)
names(exampledata)
library(glue)
library(rpart)
library(mlr3)
library(dplyr)
library(mlr3learners)
tt <- 5
t0 <- 4
yvars <- paste0('Y_-', 0:tt)
lrnc <- glue('regr.rpart')</pre>
lrnb <- glue('classif.log_reg')</pre>
tml_deltahat_s <- tmle_delta_s(data = exampledata,</pre>
                                   folds = 'ff',
                                   id = 'ID',
                                   x = 'X_0',
                                   g = 'G_0',
                                   a = paste0('A_', 0:tt),
                                   y = yvars,
                                   s = paste0('S_', 0:t0),
                                   binary_lrnr = lrn(lrnb, predict_type = 'prob'),
                                   cont_lrnr = lrn(lrnc),
```

t0=t0, truncate\_e = 0.005, verbose = FALSE)

tml\_deltahat\_s

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