

Package ‘lntp’

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Title Non-Parametric Causal Effects of Feasible Interventions Based on Modified Treatment Policies

Version 1.5.4

Description Non-parametric estimators for casual effects based on longitudinal modified treatment policies as described in Diaz, Williams, Hoffman, and Schenck <[doi:10.1080/01621459.2021.1955691](https://doi.org/10.1080/01621459.2021.1955691)>, traditional point treatment, and traditional longitudinal effects. Continuous, binary, categorical treatments, and multivariate treatments are allowed as well as censored outcomes. The treatment mechanism is estimated via a density ratio classification procedure irrespective of treatment variable type. For both continuous and binary outcomes, additive treatment effects can be calculated and relative risks and odds ratios may be calculated for binary outcomes. Supports survival outcomes with competing risks (Diaz, Hoffman, and Hejazi; <[doi:10.1007/s10985-023-09606-7](https://doi.org/10.1007/s10985-023-09606-7)>).

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event_locf	<i>Time To Event Last Outcome Carried Forward</i>
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Description

A helper function to prepare survival data for use with LMTP estimators by imputing outcome nodes using last outcome carried forward when an observation experiences the event before the end-of-follow-up.

Usage

```
event_locf(data, outcomes)
```

Arguments

data	The dataset to modify.
outcomes	A vector of outcome nodes ordered by time.

Value

A modified dataset with future outcome nodes set to 1 if an observation experienced an event at any previous time point.

Examples

```
event_locf(sim_point_surv, paste0("Y.", 1:6))
```

ipsi

IPSI Function Factory

Description

A function factory that returns a shift function for increasing or decreasing the probability of exposure when exposure is binary.

Usage

```
ipsi(delta)
```

Arguments

delta	[numeric(1)] A risk ratio between 0 and Inf.
-------	---

Value

A shift function.

See Also

[lmtp_tmle\(\)](#), [lmtp_sdr\(\)](#)

Examples

```
data("iptwExWide", package = "twang")
a <- paste0("tx", 1:3)
baseline <- c("gender", "age")
tv <- list(c("use0"), c("use1"), c("use2"))
lmtp_sdr(iptwExWide, a, "outcome", baseline = baseline, time_vary = tv,
        shift = ipsi(0.5), outcome_type = "continuous", folds = 2)
```

lmtptest

Perform Contrasts of LMTP Fits

Description

Estimates contrasts of multiple LMTP fits compared to either a known reference value or a reference LMTP fit.

Usage

```
lmtptest(..., ref, type = c("additive", "rr", "or"))
```

Arguments

... One or more objects of class lmtptest.
ref A reference value or another lmtptest fit to compare all other fits against.
type The contrasts of interest. Options are "additive" (the default), "rr", and "or".

Value

A list of class lmtptest containing the following components:

type The type of contrast performed.
null The null hypothesis.
estimates A dataframe containing the contrasts estimates, standard errors, and confidence intervals.

Examples

```
a <- c("A1", "A2")
nodes <- list(c("L1"), c("L2"))
cens <- c("C1", "C2")
y <- "Y"

# mean population outcome
psi_null <- lmtptest(sim_cens, a, y, time_vary = nodes, cens = cens, shift = NULL, folds = 1)

# treatment rule, everyone is increased by 0.5
d <- function(data, x) data[[x]] + 0.5
psi_rule1 <- lmtptest(sim_cens, a, y, time_vary = nodes, cens = cens,
  shift = d, folds = 1, mtp = TRUE)

# treatment rule, everyone is decreased by 0.5
d <- function(data, x) data[[x]] - 0.5
psi_rule2 <- lmtptest(sim_cens, a, y, time_vary = nodes, cens = cens,
  shift = d, folds = 1, mtp = TRUE)

# Example 1.1
```

```

# Additive effect of rule 1 compared to a known constant
lmtpl_contrast(psi_rule1, ref = 0.9)

# Example 1.2
# Additive effect of rule 1 compared to the population mean outcome
lmtpl_contrast(psi_rule1, ref = psi_null)

# Example 1.3
# Additive effects of rule 1 and 2 compared to the population mean outcome
lmtpl_contrast(psi_rule1, psi_rule2, ref = psi_null)

# Example 1.4
# Relative risk of rule 1 compared to observed exposure
lmtpl_contrast(psi_rule1, ref = psi_null, type = "rr")

# Example 1.5
# Odds of rule 1 compared to observed exposure
lmtpl_contrast(psi_rule1, ref = psi_null, type = "or")

```

lmtpl_control

Set LMTP Estimation Parameters

Description

Set LMTP Estimation Parameters

Usage

```

lmtpl_control(
  .bound = 1e+05,
  .trim = 0.999,
  .learners_outcome_folds = 10,
  .learners_trt_folds = 10,
  .return_full_fits = FALSE,
  .discrete = TRUE,
  .info = FALSE
)

```

Arguments

.bound	[numeric(1)] Determines that maximum and minimum values (scaled) predictions will be bounded by. The default is 1e-5, bounding predictions by 1e-5 and 0.9999.
.trim	[numeric(1)] Determines the amount the density ratios should be trimmed. The default is 0.999, trimming the density ratios greater than the 0.999 percentile to the 0.999 percentile. A value of 1 indicates no trimming.

```

.learners_outcome_folds
    [integer(1)]
    The number of cross-validation folds for learners_outcome.
.learners_trt_folds
    [integer(1)]
    The number of cross-validation folds for learners_trt.
.return_full_fits
    [logical(1)]
    Return full 'SuperLearner' fits? Default is FALSE, return only 'SuperLearner'
    coefficients.
.discrete
    [logical(1)]
    Use discrete or ensemble super learner?
.info
    [logical(1)]
    Print super learner fitting info to the console?

```

Value

A list of parameters controlling the estimation procedure.

Examples

```
lntp_control(.trim = 0.975)
```

lntp_sdr

LMTP Sequential Doubly Robust Estimator

Description

Sequentially doubly robust estimator for the effects of traditional causal effects and modified treatment policies for both point treatment and longitudinal data with binary, continuous, or time-to-event outcomes. Supports binary, categorical, and continuous exposures.

Usage

```

lntp_sdr(
  data,
  trt,
  outcome,
  baseline = NULL,
  time_vary = NULL,
  cens = NULL,
  compete = NULL,
  shift = NULL,
  shifted = NULL,
  k = Inf,
  mtp = TRUE,
  outcome_type = c("binomial", "continuous", "survival"),

```

```

    id = NULL,
    bounds = NULL,
    learners_outcome = "SL.glm",
    learners_trt = "SL.glm",
    folds = 10,
    weights = NULL,
    control = lmtpr_control()
  )

```

Arguments

data	[data.frame] A data.frame in wide format containing all necessary variables for the estimation problem. Must not be a data.table.
trt	[character] or [list] A vector containing the column names of treatment variables ordered by time. Or, a list of vectors, the same length as the number of time points of observation. Vectors should contain column names for the treatment variables at each time point. The list should be ordered following the time ordering of the model.
outcome	[character] The column name of the outcome variable. In the case of time-to-event analysis, a vector containing the columns names of intermediate outcome variables and the final outcome variable ordered by time. Only numeric values are allowed. If the outcome type is binary, data should be coded as 0 and 1.
baseline	[character] An optional vector containing the column names of baseline covariates to be included for adjustment at every time point.
time_vary	[list] A list the same length as the number of time points of observation with the column names for new time-varying covariates introduced at each time point. The list should be ordered following the time ordering of the model.
cens	[character] An optional vector of column names of censoring indicators the same length as the number of time points of observation. If missingness in the outcome is present or if time-to-event outcome, must be provided.
compete	[character] An optional vector of column names of competing risk indicators the same length as the number of time points of observation. Only used when outcome_type = "survival".
shift	[closure] A two argument function that specifies how treatment variables should be shifted. See examples for how to specify shift functions for continuous, binary, and categorical exposures.
shifted	[data.frame] An optional data frame, the same as in data, but modified according to the treatment policy of interest. If specified, shift is ignored.

k	[integer(1)] An integer specifying how previous time points should be used for estimation at the given time point. Default is Inf, all time points.
mtp	[logical(1)] Is the intervention of interest a modified treatment policy? Default is TRUE. If treatment variables are continuous this should be TRUE. If the treatment variables are not continuous, setting this to FALSE may improve performance.
outcome_type	[character(1)] Outcome variable type (i.e., continuous, binomial, survival).
id	[character(1)] An optional column name containing cluster level identifiers.
bounds	[numeric(2)] An optional, ordered vector of the bounds for a continuous outcomes. If NULL, the bounds will be taken as the minimum and maximum of the observed data. Should be left as NULL if the outcome type is binary.
learners_outcome	[character] A vector of SuperLearner algorithms for estimation of the outcome regression. Default is "SL.glm".
learners_trt	[character] A vector of SuperLearner algorithms for estimation of the outcome regression. Default is "SL.glm". Only include candidate learners capable of binary classification.
folds	[integer(1)] The number of folds to be used for cross-fitting.
weights	[numeric(nrow(data))] An optional vector containing sampling weights.
control	[list()] Output of lmtpr_control().

Details

Should mtp = TRUE?:

A modified treatment policy (MTP) is an intervention that depends on the natural value of the exposure (the value that the treatment would have taken under no intervention). This differs from other causal effects, such as the average treatment effect (ATE), where an exposure would be increased (or decreased) deterministically. **If your intervention of interest adds, subtracts, or multiplies the observed treatment values by some amount, use mtp = TRUE.**

Value

A list of class lmtpr containing the following components:

estimator	The estimator used, in this case "SDR".
estimates	The estimated population LMTP effect as an ife object.
shift	The shift function specifying the treatment policy of interest.

outcome_reg	An $n \times \text{Tau} + 1$ matrix of outcome regression predictions. The mean of the first column is used for calculating theta.
density_ratios	An $n \times \text{Tau}$ matrix of the estimated, non-cumulative, density ratios.
fits_m	A list the same length as folds, containing the fits at each time-point for each fold for the outcome regression.
fits_r	A list the same length as folds, containing the fits at each time-point for each fold of density ratio estimation.
outcome_type	The outcome variable type.

Examples

```

set.seed(56)
n <- 1000
W <- rnorm(n, 10, 5)
A <- 23 + 5*W + rnorm(n)
Y <- 7.2*A + 3*W + rnorm(n)
ex1_dat <- data.frame(W, A, Y)

# Example 1.1
# Point treatment, continuous exposure, continuous outcome, no loss-to-follow-up
# Interested in the effect of a modified treatment policy where A is decreased by 15
# units only among observations whose observed A was above 80.
# The true value under this intervention is about 513.
policy <- function(data, x) {
  (data[[x]] > 80)*(data[[x]] - 15) + (data[[x]] <= 80)*data[[x]]
}

lmtpr_sdr(ex1_dat, "A", "Y", "W", shift = policy,
          outcome_type = "continuous", folds = 2, mtp = TRUE)

# Example 2.1
# Longitudinal setting, time-varying continuous exposure bounded by 0,
# time-varying covariates, and a binary outcome with no loss-to-follow-up.
# Interested in the effect of a treatment policy where exposure decreases by
# one unit at every time point if an observations observed exposure is greater
# than or equal to 2. The true value under this intervention is about 0.305.
head(sim_t4)

A <- c("A_1", "A_2", "A_3", "A_4")
L <- list(c("L_1"), c("L_2"), c("L_3"), c("L_4"))

policy <- function(data, trt) {
  a <- data[[trt]]
  (a - 1) * (a - 1 >= 1) + a * (a - 1 < 1)
}

# BONUS: progressr progress bars!
progressr::handlers(global = TRUE)

lmtpr_sdr(sim_t4, A, "Y", time_vary = L, shift = policy,
          folds = 2, mtp = TRUE)

```

```

# Example 2.2
# The previous example assumed that the outcome (as well as the treatment variables)
# were directly affected by all other nodes in the past. In certain situations,
# domain specific knowledge may suggest otherwise.
# This can be controlled using the k argument.
lmtpr_sdr(sim_t4, A, "Y", time_vary = L, shift = policy,
          k = 0, folds = 2, mtp = TRUE)

# Example 2.3
# Using the same data as examples 2.1 and 2.2.
# Now estimating the effect of a dynamic modified treatment policy.
# creating a dynamic mtp that applies the shift function
# but also depends on history and the current time
policy <- function(data, trt) {
  mtp <- function(data, trt) {
    (data[[trt]] - 1) * (data[[trt]] - 1 >= 1) + data[[trt]] * (data[[trt]] - 1 < 1)
  }

  # if its the first time point, follow the same mtp as before
  if (trt == "A_1") return(mtp(data, trt))

  # otherwise check if the time varying covariate equals 1
  ifelse(
    data[[sub("A", "L", trt)]] == 1,
    mtp(data, trt), # if yes continue with the policy
    data[[trt]]     # otherwise do nothing
  )
}

lmtpr_sdr(sim_t4, A, "Y", time_vary = L, mtp = TRUE,
          k = 0, shift = policy, folds = 2)

# Example 2.4
# Using the same data as examples 2.1, 2.2, and 2.3, but now treating the exposure
# as an ordered categorical variable. To account for the exposure being a
# factor we just need to modify the shift function (and the original data)
# so as to respect this.
tmp <- sim_t4
for (i in A) {
  tmp[[i]] <- factor(tmp[[i]], levels = 0:5, ordered = FALSE)
}

policy <- function(data, trt) {
  out <- list()
  a <- data[[trt]]
  for (i in 1:length(a)) {
    if (as.character(a[i]) %in% c("0", "1")) {
      out[[i]] <- as.character(a[i])
    } else {
      out[[i]] <- as.numeric(as.character(a[i])) - 1
    }
  }
}

```

```

    factor(unlist(out), levels = 0:5, ordered = FALSE)
  }

lmp_sdr(tmp, A, "Y", time_vary = L, shift = policy,
        k = 0, folds = 2, mtp = TRUE)

# Example 3.1
# Longitudinal setting, time-varying binary treatment, time-varying covariates
# and baseline covariates with no loss-to-follow-up. Interested in a "traditional"
# causal effect where treatment is set to 1 at all time points for all observations.
if (require("twang")) {
  data("iptwExWide", package = "twang")

  A <- paste0("tx", 1:3)
  W <- c("gender", "age")
  L <- list(c("use0"), c("use1"), c("use2"))

  lmp_sdr(
    iptwExWide, A, "outcome", baseline = W, time_vary = L,
    shift = static_binary_on, outcome_type = "continuous",
    mtp = FALSE, folds = 2
  )
}

# Example 4.1
# Longitudinal setting, time-varying continuous treatment, time-varying covariates,
# binary outcome with right censoring. Interested in the mean population outcome under
# the observed exposures in a hypothetical population with no loss-to-follow-up.
head(sim_cens)

A <- c("A1", "A2")
L <- list(c("L1"), c("L2"))
C <- c("C1", "C2")
Y <- "Y"

lmp_sdr(sim_cens, A, Y, time_vary = L, cens = C, shift = NULL, folds = 2)

# Example 5.1
# Time-to-event analysis with a binary time-invariant exposure. Interested in
# the effect of treatment being given to all observations on the cumulative
# incidence of the outcome.
# For a survival problem, the outcome argument now takes a vector of outcomes
# if an observation experiences the event prior to the end of follow-up, all future
# outcome nodes should be set to 1 (i.e., last observation carried forward).
A <- "trt"
Y <- paste0("Y.", 1:6)
C <- paste0("C.", 0:5)
W <- c("W1", "W2")

lmp_sdr(sim_point_surv, A, Y, W, cens = C, folds = 2,
        shift = static_binary_on, outcome_type = "survival")

# Example 6.1

```

```

# Intervening on multiple exposures simultaneously. Interested in the effect of
# a modified treatment policy where variable D1 is decreased by 0.1 units and
# variable D2 is decreased by 0.5 units simultaneously.
A <- list(c("D1", "D2"))
W <- paste0("C", 1:3)
Y <- "Y"

d <- function(data, a) {
  out = list(
    data[[a[1]]] - 0.1,
    data[[a[2]]] - 0.5
  )
  setNames(out, a)
}

lmtpr_sdr(multivariate_data, A, Y, W, shift = d,
          outcome_type = "continuous", folds = 1, mtp = TRUE)

# Example 7.1
# Time-to-event analysis with a binary time-invariant exposure and a competing-risk.
lmtpr_sdr(
  data = sim_competing_risks,
  trt = "A",
  cens = paste0("C", 1:5),
  compete = paste0("D", 1:5),
  baseline = paste0("W", 1:5),
  outcome = paste0("Y", 1:5),
  outcome_type = "survival",
  shift = static_binary_on,
  folds = 1
)

```

lmtpr_survival

LMTP Survival Curve Estimator

Description

Wrapper around `lmtpr_tmle` and `lmtpr_sdr` for survival outcomes to estimate the entire survival curve. Estimates are reconstructed using isotonic regression to enforce monotonicity of the survival curve. **Confidence intervals correspond to marginal confidence intervals for the survival curve, not simultaneous intervals.**

Usage

```

lmtpr_survival(
  data,
  trt,
  outcomes,
  baseline = NULL,

```

```

time_vary = NULL,
cens = NULL,
compete = NULL,
shift = NULL,
shifted = NULL,
estimator = c("lmtpr_tmle", "lmtpr_sdr"),
k = Inf,
mtp = TRUE,
id = NULL,
learners_outcome = "SL.glm",
learners_trt = "SL.glm",
folds = 10,
weights = NULL,
control = lmtpr_control()
)

```

Arguments

data	[data.frame] A data.frame in wide format containing all necessary variables for the estimation problem. Must not be a data.table.
trt	[character] or [list] A vector containing the column names of treatment variables ordered by time. Or, a list of vectors, the same length as the number of time points of observation. Vectors should contain column names for the treatment variables at each time point. The list should be ordered following the time ordering of the model.
outcomes	[character] A vector containing the columns names of intermediate outcome variables and the final outcome variable ordered by time. Only numeric values are allowed. Variables should be coded as 0 and 1.
baseline	[character] An optional vector containing the column names of baseline covariates to be included for adjustment at every time point.
time_vary	[list] A list the same length as the number of time points of observation with the column names for new time-varying covariates introduced at each time point. The list should be ordered following the time ordering of the model.
cens	[character] An optional vector of column names of censoring indicators the same length as the number of time points of observation. If missingness in the outcome is present or if time-to-event outcome, must be provided.
compete	[character] An optional vector of column names of competing risk indicators the same length as the number of time points of observation.
shift	[closure] A two argument function that specifies how treatment variables should be shifted.

	See examples for how to specify shift functions for continuous, binary, and categorical exposures.
shifted	[data.frame] An optional data frame, the same as in data, but modified according to the treatment policy of interest. If specified, shift is ignored.
estimator	[character(1)] The estimator to use. Either "lmtpr_tmle" or "lmtpr_sdr".
k	[integer(1)] An integer specifying how previous time points should be used for estimation at the given time point. Default is Inf, all time points.
mtp	[logical(1)] Is the intervention of interest a modified treatment policy? Default is TRUE. If treatment variables are continuous this should be TRUE. If the treatment variables are not continuous, setting this to FALSE may improve performance.
id	[character(1)] An optional column name containing cluster level identifiers.
learners_outcome	[character] A vector of SuperLearner algorithms for estimation of the outcome regression. Default is "SL.glm", a main effects GLM.
learners_trt	[character] A vector of SuperLearner algorithms for estimation of the exposure mechanism. Default is "SL.glm", a main effects GLM. Only include candidate learners capable of binary classification.
folds	[integer(1)] The number of folds to be used for cross-fitting.
weights	[numeric(nrow(data))] An optional vector containing sampling weights.
control	[list()] Output of lmtpr_control().

Value

A list of class lmtpr_survival containing lmtpr objects for each time point.

Examples

```
# Example 1.1
# Time-to-event analysis with a binary time-invariant exposure. Interested in
# the effect of treatment being given to all observations on the cumulative
# incidence of the outcome.
A <- "trt"
Y <- paste0("Y.", 1:6)
C <- paste0("C.", 0:5)
W <- c("W1", "W2")

curve <- lmtpr_survival(sim_point_surv, A, Y, W, cens = C, folds = 1,
```

```

      shift = static_binary_on, estimator = "lmtpl_tmle")

tidy(curve)

# Example 1.2
# Time-to-event analysis with a binary time-invariant exposure and a competing-risk.
lmtpl_survival(
  data = sim_competing_risks,
  trt = "A",
  cens = paste0("C", 1:5),
  compete = paste0("D", 1:5),
  baseline = paste0("W", 1:5),
  outcome = paste0("Y", 1:5),
  shift = static_binary_on,
  folds = 1
)

```

lmtpl_tmle

LMTP Targeted Maximum Likelihood Estimator

Description

Targeted maximum likelihood estimator for the effects of traditional causal effects and modified treatment policies for both point treatment and longitudinal data with binary, continuous, or time-to-event outcomes. Supports binary, categorical, and continuous exposures.

Usage

```

lmtpl_tmle(
  data,
  trt,
  outcome,
  baseline = NULL,
  time_vary = NULL,
  cens = NULL,
  compete = NULL,
  shift = NULL,
  shifted = NULL,
  k = Inf,
  mtp = TRUE,
  outcome_type = c("binomial", "continuous", "survival"),
  id = NULL,
  bounds = NULL,
  learners_outcome = "SL.glm",
  learners_trt = "SL.glm",
  folds = 10,
  weights = NULL,
  control = lmtpl_control()
)

```

Arguments

data	[data.frame] A data.frame in wide format containing all necessary variables for the estimation problem. Must not be a data.table.
trt	[character] or [list] A vector containing the column names of treatment variables ordered by time. Or, a list of vectors, the same length as the number of time points of observation. Vectors should contain column names for the treatment variables at each time point. The list should be ordered following the time ordering of the model.
outcome	[character] The column name of the outcome variable. In the case of time-to-event analysis, a vector containing the columns names of intermediate outcome variables and the final outcome variable ordered by time. Only numeric values are allowed. If the outcome type is binary, data should be coded as 0 and 1.
baseline	[character] An optional vector containing the column names of baseline covariates to be included for adjustment at every time point.
time_vary	[list] A list the same length as the number of time points of observation with the column names for new time-varying covariates introduced at each time point. The list should be ordered following the time ordering of the model.
cens	[character] An optional vector of column names of censoring indicators the same length as the number of time points of observation. If missingness in the outcome is present or if time-to-event outcome, must be provided.
compete	[character] An optional vector of column names of competing risk indicators the same length as the number of time points of observation. Only used when outcome_type = "survival".
shift	[closure] A two argument function that specifies how treatment variables should be shifted. See examples for how to specify shift functions for continuous, binary, and categorical exposures.
shifted	[data.frame] An optional data frame, the same as in data, but modified according to the treatment policy of interest. If specified, shift is ignored.
k	[integer(1)] An integer specifying how previous time points should be used for estimation at the given time point. Default is Inf, all time points.
mtp	[logical(1)] Is the intervention of interest a modified treatment policy? Default is TRUE. If treatment variables are continuous this should be TRUE. If the treatment variables are not continuous, setting this to FALSE may improve performance.
outcome_type	[character(1)] Outcome variable type (i.e., continuous, binomial, survival).

id	[character(1)] An optional column name containing cluster level identifiers.
bounds	[numeric(2)] An optional, ordered vector of the bounds for a continuous outcomes. If NULL, the bounds will be taken as the minimum and maximum of the observed data. Should be left as NULL if the outcome type is binary.
learners_outcome	[character] A vector of SuperLearner algorithms for estimation of the outcome regression. Default is "SL.glm".
learners_trt	[character] A vector of SuperLearner algorithms for estimation of the outcome regression. Default is "SL.glm". Only include candidate learners capable of binary classification.
folds	[integer(1)] The number of folds to be used for cross-fitting.
weights	[numeric(nrow(data))] An optional vector containing sampling weights.
control	[list()] Output of lmtpl_control().

Details

Should mtp = TRUE?:

A modified treatment policy (MTP) is an intervention that depends on the natural value of the exposure (the value that the treatment would have taken under no intervention). This differs from other causal effects, such as the average treatment effect (ATE), where an exposure would be increased (or decreased) deterministically. **If your intervention of interest adds, subtracts, or multiplies the observed treatment values by some amount, use mtp = TRUE.**

Value

A list of class lmtpl containing the following components:

estimator	The estimator used, in this case "TMLE".
estimates	The estimated population LMTP effect as an ife object.
shift	The shift function specifying the treatment policy of interest.
outcome_reg	An $n \times \text{Tau} + 1$ matrix of outcome regression predictions. The mean of the first column is used for calculating theta.
density_ratios	An $n \times \text{Tau}$ matrix of the estimated, non-cumulative, density ratios.
fits_m	A list the same length as folds, containing the fits at each time-point for each fold for the outcome regression.
fits_r	A list the same length as folds, containing the fits at each time-point for each fold of density ratio estimation.
outcome_type	The outcome variable type.

Examples

```

set.seed(56)
n <- 1000
W <- rnorm(n, 10, 5)
A <- 23 + 5*W + rnorm(n)
Y <- 7.2*A + 3*W + rnorm(n)
ex1_dat <- data.frame(W, A, Y)

# Example 1.1
# Point treatment, continuous exposure, continuous outcome, no loss-to-follow-up
# Interested in the effect of a modified treatment policy where A is decreased by 15
# units only among observations whose observed A was above 80.
# The true value under this intervention is about 513.
policy <- function(data, x) {
  (data[[x]] > 80)*(data[[x]] - 15) + (data[[x]] <= 80)*data[[x]]
}

lmtp_tmle(ex1_dat, "A", "Y", "W", shift = policy,
          outcome_type = "continuous", folds = 2, mtp = TRUE)

# Example 2.1
# Longitudinal setting, time-varying continuous exposure bounded by 0,
# time-varying covariates, and a binary outcome with no loss-to-follow-up.
# Interested in the effect of a treatment policy where exposure decreases by
# one unit at every time point if an observations observed exposure is greater
# than or equal to 2. The true value under this intervention is about 0.305.
head(sim_t4)

A <- c("A_1", "A_2", "A_3", "A_4")
L <- list(c("L_1"), c("L_2"), c("L_3"), c("L_4"))
policy <- function(data, trt) {
  a <- data[[trt]]
  (a - 1) * (a - 1 >= 1) + a * (a - 1 < 1)
}

# BONUS: progressr progress bars!
progressr::handlers(global = TRUE)

lmtp_tmle(sim_t4, A, "Y", time_vary = L, shift = policy,
          folds = 2, mtp = TRUE)

# Example 2.2
# The previous example assumed that the outcome (as well as the treatment variables)
# were directly affected by all other nodes in the past. In certain situations,
# domain specific knowledge may suggest otherwise.
# This can be controlled using the k argument.
lmtp_tmle(sim_t4, A, "Y", time_vary = L, shift = policy,
          k = 0, folds = 2, mtp = TRUE)

# Example 2.3
# Using the same data as examples 2.1 and 2.2.
# Now estimating the effect of a dynamic modified treatment policy.

```

```

# creating a dynamic mtp that applies the shift function
# but also depends on history and the current time
policy <- function(data, trt) {
  mtp <- function(data, trt) {
    (data[[trt]] - 1) * (data[[trt]] - 1 >= 1) + data[[trt]] * (data[[trt]] - 1 < 1)
  }

  # if its the first time point, follow the same mtp as before
  if (trt == "A_1") return(mtp(data, trt))

  # otherwise check if the time varying covariate equals 1
  ifelse(
    data[[sub("A", "L", trt)]] == 1,
    mtp(data, trt), # if yes continue with the policy
    data[[trt]]     # otherwise do nothing
  )
}

lmtm_tml(sim_t4, A, "Y", time_vary = L, mtp = TRUE,
         k = 0, shift = policy, folds = 2)

# Example 2.4
# Using the same data as examples 2.1, 2.2, and 2.3, but now treating the exposure
# as an ordered categorical variable. To account for the exposure being a
# factor we just need to modify the shift function (and the original data)
# so as to respect this.
tmp <- sim_t4
for (i in A) {
  tmp[[i]] <- factor(tmp[[i]], levels = 0:5, ordered = FALSE)
}

policy <- function(data, trt) {
  out <- list()
  a <- data[[trt]]
  for (i in 1:length(a)) {
    if (as.character(a[i]) %in% c("0", "1")) {
      out[[i]] <- as.character(a[i])
    } else {
      out[[i]] <- as.numeric(as.character(a[i])) - 1
    }
  }
  factor(unlist(out), levels = 0:5, ordered = FALSE)
}

lmtm_tml(tmp, A, "Y", time_vary = L, shift = policy,
         k = 0, folds = 2, mtp = TRUE)

# Example 3.1
# Longitudinal setting, time-varying binary treatment, time-varying covariates
# and baseline covariates with no loss-to-follow-up. Interested in a "traditional"
# causal effect where treatment is set to 1 at all time points for all observations.
if (require("twang")) {
  data("iptwExWide", package = "twang")
}

```

```

A <- paste0("tx", 1:3)
W <- c("gender", "age")
L <- list(c("use0"), c("use1"), c("use2"))

lmtm_tmle(iptwExWide, A, "outcome", baseline = W, time_vary = L,
          shift = static_binary_on, outcome_type = "continuous",
          mtp = FALSE, folds = 2)
}

# Example 4.1
# Longitudinal setting, time-varying continuous treatment, time-varying covariates,
# binary outcome with right censoring. Interested in the mean population outcome under
# the observed exposures in a hypothetical population with no loss-to-follow-up.
head(sim_cens)

A <- c("A1", "A2")
L <- list(c("L1"), c("L2"))
C <- c("C1", "C2")
Y <- "Y"

lmtm_tmle(sim_cens, A, Y, time_vary = L, cens = C, shift = NULL, folds = 2)

# Example 5.1
# Time-to-event analysis with a binary time-invariant exposure. Interested in
# the effect of treatment being given to all observations on the cumulative
# incidence of the outcome.
# For a survival problem, the outcome argument now takes a vector of outcomes
# if an observation experiences the event prior to the end of follow-up, all future
# outcome nodes should be set to 1 (i.e., last observation carried forward).
A <- "trt"
Y <- paste0("Y.", 1:6)
C <- paste0("C.", 0:5)
W <- c("W1", "W2")

lmtm_tmle(sim_point_surv, A, Y, W, cens = C, folds = 2,
          shift = static_binary_on, outcome_type = "survival")

# Example 6.1
# Intervening on multiple exposures simultaneously. Interested in the effect of
# a modified treatment policy where variable D1 is decreased by 0.1 units and
# variable D2 is decreased by 0.5 units simultaneously.
A <- list(c("D1", "D2"))
W <- paste0("C", 1:3)
Y <- "Y"

d <- function(data, a) {
  out = list(
    data[[a[1]]] - 0.1,
    data[[a[2]]] - 0.5
  )
  setNames(out, a)
}

```

```
lmtmle(multivariate_data, A, Y, W, shift = d,
       outcome_type = "continuous", folds = 1, mtp = TRUE)

# Example 7.1
# Time-to-event analysis with a binary time-invariant exposure and a competing-risk.
lmtmle(
  data = sim_competing_risks,
  trt = "A",
  cens = paste0("C", 1:5),
  compete = paste0("D", 1:5),
  baseline = paste0("W", 1:5),
  outcome = paste0("Y", 1:5),
  outcome_type = "survival",
  shift = static_binary_on,
  folds = 1
)
```

multivariate_data	<i>Simulated Multivariate Exposure Data</i>
-------------------	---

Description

A dataset with a continuous outcome, three baseline covariates, and two treatment variables.

Usage

```
multivariate_data
```

Format

A data frame with 2000 rows and 6 variables:

C1 Continuous baseline variable.

C2 Continuous baseline variable.

C3 Continuous baseline variable.

D1 Treatment variable one at baseline.

D2 Treatment variable two at baseline.

Y Continuous outcome

`sim_cens`*Simulated Longitudinal Data With Censoring*

Description

A dataset with a binary outcome, two time varying treatment nodes, two time varying covariates, and two censoring indicators.

Usage`sim_cens`**Format**

A data frame with 1000 rows and 10 variables:

L1 Time varying covariate time 1

A1 Treatment node at time 1, effected by L_1

C1 Censoring indicator that the observation is observed after time 1

L2 Time varying covariate at time 2, effected by L_1 and A_1

A2 Treatment node at time 2, effected by L_2 and A_1

C2 Censoring indicator that the observation is observed after time 2

Y Binary outcome at time 3, effected by L_2 and A_2

`sim_competing_risks`*Simulated Competing Risks Data*

Description

A dataset with a time-to-event outcome, a competing risk, and point-treatment.

Usage`sim_competing_risks`**Format**

A data frame with 1000 rows and 21 variables.

sim_point_surv	<i>Simulated Point-treatment Survival Data</i>
----------------	--

Description

A dataset with a time-to-event outcome, two baseline nodes, a binary point treatment, six past-time outcome nodes, and six censoring indicators.

Usage

```
sim_point_surv
```

Format

A data frame with 2000 rows and 16 variables:

W1 Binary baseline variable.

W2 Categorical baseline variable.

trt Binary treatment variable.

C.0 Censoring indicator that the observation is observed future time points.

Y.1 Outcome node at time 1.

C.1 Censoring indicator that the observation is observed future time points.

Y.2 Outcome node at time 2.

C.2 Censoring indicator that the observation is observed future time points.

Y.3 Outcome node at time 3.

C.3 Censoring indicator that the observation is observed future time points.

Y.4 Outcome node at time 4.

C.4 Censoring indicator that the observation is observed future time points.

Y.5 Outcome node at time 5.

C.5 Censoring indicator that the observation is observed future time points.

Y.6 Final outcome node.

`sim_t4`*Simulated Longitudinal Data*

Description

A dataset with a binary outcome, four time varying treatment nodes, and four time varying covariates.

Usage`sim_t4`**Format**

A data frame with 5000 rows and 10 variables:

ID observation ID

L_1 Time varying covariate time 1

A_1 Treatment node at time 1, effected by L_1

L_2 Time varying covariate time 1, effected by L_1 and A_1

A_2 Treatment node at time 2, effected by L_2 and A_1

L_3 Time varying covariate time 1, effected by L_2 and A_2

A_3 Treatment node at time 3, effected by L_3 and A_2

L_4 Time varying covariate time 1, effected by L_3 and A_3

A_4 Treatment node at time 3, effected by L_4 and A_3

Y Binary outcome at time 5, effected by L_4 and A_4

`sim_timevary_surv`*Simulated Time-varying Survival Data*

Description

A dataset with a time-to-event outcome, one baseline nodes, two time-varying covariates, a binary time-varying treatment, two outcome nodes, and two censoring indicators. Data-generating mechanism taken from Lendle, Schwab, Petersen, and van der Laan (<https://www.jstatsoft.org/article/view/v081i01>).

Usage`sim_timevary_surv`

Format

A data frame with 500 rows and 11 variables:

L0.a Continuous baseline variable.

L0.b Time varying covariate at baseline.

L0.c Time varying covariate at baseline.

A0 Treatment variable at baseline

C0 Censoring indicator that the observation is observed future time points.

L1.a Time varying covariate at time 1.

L1.b Time varying covariate at time 1.

Y1 Outcome node at time 1.

A1 Treatment variable at time 1.

C1 Censoring indicator that the observation is observed future time points.

Y2 Final outcome node.

static_binary_off	<i>Turn All Treatment Nodes Off</i>
-------------------	-------------------------------------

Description

A pre-packaged shift function for use with provided estimators when the exposure is binary. Used to estimate the population intervention effect when all treatment variables are set to 0.

Usage

```
static_binary_off(data, trt)
```

Arguments

data	A dataframe containing the treatment variables.
trt	The name of the current treatment variable.

Value

A dataframe with all treatment nodes set to 0.

See Also

[lntp_tmle\(\)](#), [lntp_sdr\(\)](#)

Examples

```
data("iptwExWide", package = "twang")
a <- paste0("tx", 1:3)
baseline <- c("gender", "age")
tv <- list(c("use0"), c("use1"), c("use2"))
lmtpr_sdr(iptwExWide, a, "outcome", baseline = baseline, time_vary = tv,
          shift = static_binary_off, outcome_type = "continuous", folds = 2)
```

static_binary_on	<i>Turn All Treatment Nodes On</i>
------------------	------------------------------------

Description

A pre-packaged shift function for use with provided estimators when the exposure is binary. Used to estimate the population intervention effect when all treatment variables are set to 1.

Usage

```
static_binary_on(data, trt)
```

Arguments

data	A dataframe containing the treatment variables.
trt	The name of the current treatment variable.

Value

A dataframe with all treatment nodes set to 1.

See Also

[lmtpr_tmle\(\)](#), [lmtpr_sdr\(\)](#)

Examples

```
data("iptwExWide", package = "twang")
a <- paste0("tx", 1:3)
baseline <- c("gender", "age")
tv <- list(c("use0"), c("use1"), c("use2"))
lmtpr_sdr(iptwExWide, a, "outcome", baseline = baseline, time_vary = tv,
          shift = static_binary_on, outcome_type = "continuous", folds = 2)
```

tidy.lmtp	<i>Tidy a(n) lmtp object</i>
-----------	------------------------------

Description

Tidy a(n) lmtp object

Usage

```
## S3 method for class 'lmtp'
tidy(x, ...)
```

Arguments

x	A lmtp object produced by a call to lmtp_tmle() , lmtp_sdr() , lmtp_survival() .
...	Unused, included for generic consistency only.

Examples

```
a <- c("A1", "A2")
nodes <- list(c("L1"), c("L2"))
cens <- c("C1", "C2")
y <- "Y"
fit <- lmtp_tmle(sim_cens, a, y, time_vary = nodes, cens = cens, shift = NULL, folds = 2)
tidy(fit)
```

tidy.lmtp_survival	<i>Tidy a(n) lmtp_survival object</i>
--------------------	---------------------------------------

Description

Tidy a(n) lmtp_survival object

Usage

```
## S3 method for class 'lmtp_survival'
tidy(x, ...)
```

Arguments

x	A lmtp_survival object produced by a call to lmtp_survival() .
...	Unused, included for generic consistency only.

Examples

```
# Example 1.1
# Time-to-event analysis with a binary time-invariant exposure. Interested in
# the effect of treatment being given to all observations on the cumulative
# incidence of the outcome.
A <- "trt"
Y <- paste0("Y.", 1:6)
C <- paste0("C.", 0:5)
W <- c("W1", "W2")

curve <- lmtp_survival(sim_point_surv, A, Y, W, cens = C, folds = 1,
                      shift = static_binary_on, estimator = "lmtp_tmle")

tidy(curve)

# Example 1.2
# Time-to-event analysis with a binary time-invariant exposure and a competing-risk.
lmtp_survival(
  data = sim_competing_risks,
  trt = "A",
  cens = paste0("C", 1:5),
  compete = paste0("D", 1:5),
  baseline = paste0("W", 1:5),
  outcome = paste0("Y", 1:5),
  shift = static_binary_on,
  folds = 1
)
```

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