

Package ‘twoStageDesignTMLE’

May 8, 2026

Title Targeted Maximum Likelihood Estimation for Two-Stage Study Design

Version 1.0.1.2

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Description An inverse probability of censoring weighted (IPCW) targeted maximum likelihood estimator (TMLE) for evaluating a marginal point treatment effect from data where some variables were collected on only a subset of participants using a two-stage design (or marginal mean outcome for a single arm study). A TMLE for conditional parameters defined by a marginal structural model (MSM) is also available.

Depends tmle (>= 2.0)

Suggests dbarts (>= 0.9-18), glmnet

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Encoding UTF-8

RoxygenNote 7.3.2

NeedsCompilation no

Repository CRAN

Date/Publication 2025-02-05 16:00:02 UTC

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estimatePi	<i>estimatePi</i>
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Description

Typically not called directly by the user. Function for modeling the two-stage missingness mechanism and evaluating conditional probabilities for each observation

Usage

```
estimatePi(
  Y,
  A,
  W,
  condSetNames,
  W.Q,
  Delta.W,
  V.msm = NULL,
  pi.form,
  pi.SL.library,
  id,
  V,
  discreteSL,
  verbose,
  pi = NULL,
  obsWeights = rep(1, nrow(W))
)
```

Arguments

Y	outcome
A	binary treatment indicator
W	covariate matrix observed on everyone
condSetNames	Variables to include as predictors of missingness in <code>W.stage2</code> , any combination of Y, A, and either W (for all covariates in W) or individual covariate names in W
W.Q	additional covariates based on preliminary outcome regression
Delta.W	binary indicator of missing second stage covariates
V.msm	optional additional covariates to condition on beyond W
pi.form	parametric regression formula for estimating pi
pi.SL.library	super learner library for estimating pi
id	Identifier of independent units of observation, e.g., clusters
V	number of cross validation folds for estimating pi using super learner
discreteSL	Use discrete super learning when TRUE, otherwise ensemble super learning

verbose	When TRUE prints informational messages
pi	optional vector of user-specified probabilities
obsWeights	optional weights for evaluating pi

Value

list containing the predicted probabilities, estimation method coefficients in parametric regression model (if piform supplied), indicator of whether discrete or ensemble SL was used.

evalAugW	<i>.evalAugW calls TMLE to use super learner to evaluate preliminary predictions for $Q(0,W)$ and $Q(1,W)$ conditioning on stage 1 covariates</i>
----------	---

Description

.evalAugW calls TMLE to use super learner to evaluate preliminary predictions for $Q(0,W)$ and $Q(1,W)$ conditioning on stage 1 covariates

Usage

```
evalAugW(Y, A, W, Delta, id, family, SL.library)
```

Arguments

Y	outcome vector
A	binary treatment indicator
W	covariate matrix
Delta	outcome missingness indicator
id	identifier of i.i.d. unit
family	outcome regression family
SL.library	super learner library for outcome regression modeling

Value

W.Q, nx2 matrix of outcome predictions based on stage 1 covariates

```
print.summary.twoStageTMLE
      print.summary.twoStageTMLE
```

Description

print.summary.twoStageTMLE

Usage

```
## S3 method for class 'summary.twoStageTMLE'
print(x, ...)
```

Arguments

x an object of class summary.twoStageTMLE
 ... additional arguments (i)

Value

print object

```
print.twoStageTMLE    print.twoStageTMLE
```

Description

print.twoStageTMLE

Usage

```
## S3 method for class 'twoStageTMLE'
print(x, ...)
```

Arguments

x an object of class twoStageTMLE
 ... additional arguments (i)

Value

print tmle results using print.tmle method from tmle package

setV	<i>Utilities setV Set the number of cross-validation folds as a function of effective sample size See Phillips 2023 doi.org/10.1093/ije/dyad023</i>
------	---

Description

Utilities setV Set the number of cross-validation folds as a function of effective sample size See Phillips 2023 doi.org/10.1093/ije/dyad023

Usage

```
setV(n.effective)
```

Arguments

n.effective the effective sample size

Value

the number of cross-validation folds

summary.twoStage	<i>summary.twoStageTMLE</i>
------------------	-----------------------------

Description

Summarizes estimation procedure for missing 2nd stage covariates

Usage

```
## S3 method for class 'twoStage'
summary(object, ...)
```

Arguments

object An object of class twoStageTMLE
 ... Other arguments passed to the tmle function in the tmle package

Value

A list containing the missingness model, terms, coefficients, type,

```
summary.twoStageTMLE  summary.twoStageTMLE
```

Description

```
summary.twoStageTMLE
```

Usage

```
## S3 method for class 'twoStageTMLE'
summary(object, ...)
```

Arguments

```
object      an object of class twoStageTMLE
...         additional arguments (ignored)
```

Value

list summarizing the two-stage procedure components, summary of the twoStage missingness estimation summary of the tmle for estimating the parameter

```
twoStageDesignTMLENews
      twoStageDesignTMLENews Get news about recent updates and bug fixes
```

Description

```
twoStageDesignTMLENews Get news about recent updates and bug fixes
```

Usage

```
twoStageDesignTMLENews(...)
```

Arguments

```
...         ignored
```

Value

invisible character string giving the path to the file found.

twoStageTMLE	<i>twoStageTMLE</i>
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Description

Inverse probability of censoring weighted TMLE for evaluating parameters when the full set of covariates is available on only a subset of observations.

Usage

```
twoStageTMLE(
  Y,
  A,
  W,
  Delta.W,
  W.stage2,
  Z = NULL,
  Delta = rep(1, length(Y)),
  pi = NULL,
  piform = NULL,
  pi.SL.library = c("SL.glm", "SL.gam", "SL.glmnet", "tmle.SL.dbarts.k.5"),
  V.pi = 10,
  pi.discreteSL = TRUE,
  condSetNames = c("A", "W", "Y"),
  id = NULL,
  Q.family = "gaussian",
  augmentW = TRUE,
  augW.SL.library = c("SL.glm", "SL.glmnet", "tmle.SL.dbarts2"),
  rareOutcome = FALSE,
  verbose = FALSE,
  ...
)
```

Arguments

Y	outcome
A	binary treatment indicator
W	covariate matrix observed on everyone
Delta.W	binary indicator of missing second stage covariates
W.stage2	matrix of second stage covariates observed on subset of observations
Z	optional mediator of treatment effect for evaluating a controlled direct effect
Delta	binary indicator of missing value for outcome Y
pi	optional vector of missingness probabilities for W.stage2
piform	parametric regression formula for estimating pi (see Details)

<code>pi.SL.library</code>	super learner library for estimating π (see Details)
<code>V.pi</code>	number of cross validation folds for estimating π using super learner
<code>pi.discreteSL</code>	Use discrete super learning when TRUE, otherwise ensemble super learning
<code>condSetNames</code>	Variables to include as predictors of missingness in <code>W.stage2</code> , any combination of <code>Y</code> , <code>A</code> , and either <code>W</code> (for all covariates in <code>W</code>), or individual covariate names in <code>W</code>
<code>id</code>	Identifier of independent units of observation, e.g., clusters
<code>Q.family</code>	Regression family for the outcome
<code>augmentW</code>	When TRUE include predicted values for the outcome the set of covariates used to model the propensity score
<code>augW.SL.library</code>	super learner library for preliminary outcome regression model (ignored when <code>augmentW</code> is FALSE)
<code>rareOutcome</code>	When TRUE specifies less ambitious SL for <code>Q</code> in call to <code>tmle</code> (<code>discreteSL</code> , <code>glm</code> , <code>glmnet</code> , <code>bart</code> library, <code>V=20</code>)
<code>verbose</code>	When TRUE prints informational messages
<code>...</code>	other parameters passed to the <code>tmle</code> function (not checked)

Details

When using `piform` to specify a parametric model for π that conditions on the outcome use `Delta.W` as the dependent variable and `Y.orig` on the right hand side of the formula instead of `Y`. When writing a user-defined SL wrapper for inclusion in `pi.SL.library` use `Y` on the left hand side of the formula. If specific covariate names are used on the right hand side use `Y.orig` to condition on the outcome.

Value

object of class 'twoStageTMLE'.

<code>tmle</code>	Treatment effect estimates and summary information
<code>twoStage</code>	IPCW weight estimation summary, π are the probabilities, <code>coef</code> are SL weights or coefficients from <code>glm</code> fit, type of estimation procedure, <code>discreteSL</code> flag indicating whether discrete super learning was used
<code>augW</code>	Matrix of predicted outcomes based on stage 1 covariates only

See Also

- [tmle::tmle\(\)](#) for details on customizing the estimation procedure
- [twoStageTMLEmsm\(\)](#) for estimating conditional effects
- S Rose and MJ van der Laan. A Targeted Maximum Likelihood Estimator for Two-Stage Designs. *Int J Biostat.* 2011 Jan 1; 7(1): 17. doi:10.2202/15574679.1217

Examples

```

n <- 1000
W1 <- rnorm(n)
W2 <- rnorm(n)
W3 <- rnorm(n)
A <- rbinom(n, 1, plogis(-1 + .2*W1 + .3*W2 + .1*W3))
Y <- 10 + A + W1 + W2 + A*W1 + W3 + rnorm(n)
d <- data.frame(Y, A, W1, W2, W3)
# Set 400 with data on W3, more likely if W1 > 1
n.sample <- 400
p.sample <- 0.5 + .2*(W1 > 1)
rows.sample <- sample(1:n, size = n.sample, p = p.sample)
Delta.W <- rep(0,n)
Delta.W[rows.sample] <- 1
W3.stage2 <- cbind(W3 = W3[Delta.W==1])
#1. specify parametric models and do not augment W (fast, but not recommended)
result1 <- twoStageTMLE(Y=Y, A=A, W=cbind(W1, W2), Delta.W = Delta.W,
  W.stage2 = W3.stage2, piform = "Delta.W~ I(W1 > 0) + Y.orig", V.pi= 5,
  verbose = TRUE, Qform = "Y~A+W1",gform="A~W1 + W2 +W3", augmentW = FALSE)
summary(result1)

#2. specify a parametric model for conditional missingness probabilities (pi)
# and use default values to estimate marginal effect using \code{tmle}
result2 <- twoStageTMLE(Y=Y, A=A, W=cbind(W1, W2), Delta.W = Delta.W,
  W.stage2 = cbind(W3)[Delta.W == 1], piform = "Delta.W~ I(W1 > 0)",
  V.pi= 5,verbose = TRUE)
result2

```

twoStageTMLEmsm

twoStageTMLEmsm

Description

Inverse probability of censoring weighted TMLE for evaluating MSM parameters when the full set of covariates is available on only a subset of observations, as in a 2-stage design.

Usage

```

twoStageTMLEmsm(
  Y,
  A,
  W,
  V,
  Delta.W,
  W.stage2,
  Delta = rep(1, length(Y)),
  pi = NULL,
  piform = NULL,

```

```

pi.SL.library = c("SL.glm", "SL.gam", "SL.glmnet", "tmle.SL.dbarts.k.5"),
V.pi = 10,
pi.discreteSL = TRUE,
condSetNames = c("A", "V", "W", "Y"),
id = NULL,
Q.family = "gaussian",
augmentW = TRUE,
augW.SL.library = c("SL.glm", "SL.glmnet", "tmle.SL.dbarts2"),
rareOutcome = FALSE,
verbose = FALSE,
...
)

```

Arguments

Y	outcome of interest (missingness allowed)
A	binary treatment indicator
W	matrix or data.frame of covariates measured on entire population
V	vector, matrix, or dataframe of covariates used to define MSM strata
Delta.W	Indicator of inclusion in subset with additional information
W.stage2	matrix or data.frame of covariates measured in subset population
Delta	binary indicator that outcome Y is observed
pi	optional vector of sampling probabilities
piform	parametric regression formula for estimating pi (see Details)
pi.SL.library	super learner library for estimating pi (see Details)
V.pi	optional number of cross-validation folds for super learning (ignored when pi-form or pi is provided)
pi.discreteSL	flag to indicate whether to use ensemble or discrete super learning (ignored when pi-form or pi is provided)
condSetNames	Variables to include as predictors of missingness in W.stage2, any combination of Y, A, and either W (for all covariates in W), or individual covariate names in W
id	optional indicator of independent units of observation
Q.family	outcome regression family, "gaussian" or "binomial"
augmentW	set to TRUE to augment W with predicted outcome values when A = 0 and A = 1
augW.SL.library	super learner library for preliminary outcome regression model (ignored when augmentW is FALSE)
rareOutcome	when TRUE sets V.Q = 20, Q.discreteSL = TRUE, Q.SL.library includes glm, glmnet, bart
verbose	when TRUE prints informative messages
...	other arguments passed to the tmleMSM function

Details

When using `pi`form to specify a parametric model for π that conditions on the outcome use `Delta.W` as the dependent variable and `Y.orig` on the right hand side of the formula instead of `Y`. When writing a user-defined SL wrapper for inclusion in `pi.SL.library` use `Y` on the left hand side of the formula. If specific covariate names are used on the right hand side use `Y.orig` to condition on the outcome.

Value

Object of class "twoStageTMLE"

Treatment effect estimates and summary information from call to `tmleMSM` function

tmleStage IPCW weight estimation summary, `pi` are the probabilities, `coef` are SL weights or coefficients from `glm` fit, `type` of estimation procedure, `discreteSL` flag indicating whether discrete super learning was used

augW Matrix of predicted outcomes based on stage 1 covariates only

See Also

- `tmle::tmleMSM()` for details on customizing the estimation procedure
- `twoStageTMLE()` for estimating marginal effects

Examples

```
n <- 1000
set.seed(10)
W1 <- rnorm(n)
W2 <- rnorm(n)
W3 <- rnorm(n)
A <- rbinom(n, 1, plogis(-1 + .2*W1 + .3*W2 + .1*W3))
Y <- 10 + A + W1 + W2 + A*W1 + W3 + rnorm(n)
Y.bin <- rbinom(n, 1, plogis(-4.6 - 1.8* A + W1 + W2 -.3 *A*W1 + W3))
# Set 400 obs with data on W3, more likely if W1 > 1
n.sample <- 400
p.sample <- 0.5 + .2*(W1 > 1)
rows.sample <- sample(1:n, size = n.sample, p = p.sample)
Delta.W <- rep(0,n)
Delta.W[rows.sample] <- 1
W3.stage2 <- cbind(W3 = W3[Delta.W==1])

# 1. specify parametric models, misspecified outcome model (not recommended)
result1.MSM <- twoStageTMLEmsm(Y=Y, A=A, V= cbind(W1), W=cbind(W2),
Delta.W = Delta.W, W.stage2 = W3.stage2, augmentW = FALSE,
piform = "Delta.W~ I(W1 > 0)", MSM = "A*W1", augW.SL.library = "SL.glm",
Qform = "Y~A+W1", gform="A~W1 + W2 +W3", hAVform = "A~1", verbose=TRUE)
summary(result1.MSM)

# 2. Call again, passing in previously estimated observation weights,
# note that specifying a correct model for Q improves efficiency
result2.MSM <- twoStageTMLEmsm(Y=Y, A=A, V= cbind(W1), W=cbind(W2),
Delta.W = Delta.W, W.stage2 = W3.stage2, augmentW = FALSE,
```

```
pi = result1.MSM$twoStage$pi, MSM = "A*W1",  
Qform = "Y~ A + W1 + W2 + A*W1 + W3", gform="A~W1 + W2 +W3", hAVform = "A~1")  
cbind(SE.Qmis = result1.MSM$tmle$se, SE.Qcor = result2.MSM$tmle$se)
```

```
#Binary outcome, augmentW, rareOutcome  
result3.MSM <- twoStageTMLEmsm(Y=Y.bin, A=A, V= cbind(W1), W=cbind(W2),  
Delta.W = Delta.W, W.stage2 = W3.stage2, augmentW = TRUE,  
piform = "Delta.W~ I(W1 > 0)", MSM = "A*W1", gform="A~W1 + W2 +W3",  
Q.family = "binomial", rareOutcome=TRUE)
```

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