Package ‘tLagPropOdds’

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Author Marie Davidian [aut],
      A. A. Tsiatis [aut],
      Shannon T. Holloway [aut, cre]
Maintainer Shannon T. Holloway <sthollow@ncsu.edu>
Description Implements a semiparametric estimator for the odds ratio model with censored, time-lagged, ordered categorical outcome in a randomized clinical trial that incorporates baseline and time-dependent information.
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**Description**

Inverse probability weighted complete case (IPWCC) and augmented inverse probability weighted complete case (AIPWCC) estimators for the probability of falling into a specific time-lagged ordered categorical outcome in a randomized clinical trial.

**Usage**

```r
catProbs(data, ..., ti = NULL, td = NULL)
```

**Arguments**

- `data` A data.frame object. A data.frame containing all observed data. At a minimum, this data.frame must contain columns with headers "id", "U", "delta", "Cat" and "A". If the time-independent component of the estimator is to be included, data.frame must also contain the bases of f(X). If the time-dependent component is included, data.frame must also contain the bases of h(X,L) as well as the time intervals with column headers {"tstart", "tstop"} or {"start","stop"}. See Details for additional information.
- `...` Ignored. Included to require named inputs.
- `ti` A character or integer vector or NULL. The columns of data to be included in the time-independent component of the estimator, f_m(X) m = 0, ..., M. If NULL, the time-independent component is excluded from the AIPWCC estimator. See Details for additional information.
- `td` A character or integer vector or NULL. The columns of data to be included in the time-dependent component of the estimator, h_l(X,Lbar), l = 1, ..., L. If NULL, the time-dependent component is excluded from the AIPWCC estimator. See Details for additional information.

**Details**

At a minimum, the data provided for the analysis must contain the following information:

- **id**: A unique participant identifier.
- **U**: The time to ascertainment of category or censoring.
- **delta**: The indicator of ascertainment of category (1 if U is the time to ascertainment; 0 otherwise).
- **Cat**: The ordered outcome category. Data must be provided as a factor or an integer or be able to be converted to an integer without loss of information. If participant was censored (delta = 0), Cat can take any integer-like value or NA.
- **A**: The treatment received. Data must be provided as a factor or an integer or be able to be converted to an integer without loss of information.
With the exception of Cat, data must be complete.

If the time-independent component is to be included in the AIPWCC estimator, data must also include the time-independent basis functions \( f_m(X) \ m = 0, ..., M \). If the intercept (\( f_0 \)) term is not provided, it will be added by the software.

If the time-dependent component is to be included in the AIPWCC estimator, the data.frame must be a time-dependent dataset as described by package survival. Specifically, the time-dependent data must be specified for intervals \([\text{start}, \text{stop}]\), and the data must include the following additional columns:

- **tstart**: The lower boundary of the time interval to which the data pertain.
- **tstop**: The upper boundary of the time interval to which the data pertain.

Note that column headers {"start", "stop"} are also accepted.

The various combinations of inputs \( \text{ti} \) and \( \text{td} \) yield the following:

- \( \text{ti} = \text{NULL, td = NULL} \) the IPWCC estimate is returned. (denoted as IPW in the simulations of the original manuscript.)
- \( \text{ti} \neq \text{NULL, td \neq NULL} \) the IPWCC and the full AIPWCC estimates are returned. (denoted as AIPW2 in the simulations of the original manuscript.)
- \( \text{ti} = \text{NULL, td \neq NULL} \) the IPWCC and the partial, time-independent AIPWCC estimates are returned. (denoted as AIPW1 in the simulations of the original manuscript.)
- \( \text{ti} = \text{NULL, td } \neq \text{NULL} \) the IPWCC and the partial, time-dependent AIPWCC estimates are returned.

If a treatment subgroup has <5% censoring, a message is generated and the treatment subgroup is removed from the time-dependent component of the AIPWCC estimator. If there is no censoring, the IPWCC estimator approaches the usual proportional odds estimator.

**Value**

An S3 object of class catProbsObj containing a list. The elements of the list correspond to the selected AIPWCC and/or IPWCC estimators. For each estimator, a list of matrix objects is returned, one for each treatment, that contains the estimated probabilities, their asymptotic standard errors, and the 95% confidence intervals. The S3 object has an additional attribute, "type", giving a verbose description of the components contained in the estimator.

**Examples**

```
data(tLagData)

# full AIPWCC estimator
catProbs(data = tLagData, ti = "x", td = c("hospStatus", "daysOut"))

# partial, time-independent AIPWCC estimator
catProbs(data = tLagData, ti = "x")

# partial, time-dependent AIPWCC estimator
catProbs(data = tLagData, td = c("hospStatus", "daysOut"))
```
Print Analysis Results

Description

Prints the key results.

Usage

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

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

Arguments

- `x`: A tLagObj object. The value returned by tLagPropOdds().
- `...`: Ignored.

Examples

```r
data(tLagData)

# full AIPWCC estimator
res <- catProbs(data = tLagData,
                ti = "x",
                td = c("hospStatus", "daysOut"))

print(x = res)

data(tLagData)

# full AIPWCC estimator
res <- tLagPropOdds(data = tLagData,
                   ti = "x",
                   td = c("hospStatus", "daysOut"))

print(x = res)
```
Description

These data are provided for the purposes of illustrating the use of the software. Though the data were generated under a scenario similar to a real-world COVID-19 therapeutics clinical trial, they should not be interpreted as representing true clinical trial data.

Usage

data(tLagData)

Format

tLagData is a time-dependent data.frame containing the following information for 602 participants ascertained at day 90 of a fictitious randomized clinical trial.

id: A unique participant identifier.
A: The treatment received, where A=0,1.
Cat: The ordered outcome category. There are 6 categories ascertained at day 90.
  1: at home and off oxygen, number of days >= 77;
  2: at home and off oxygen, number of days 49-76;
  3: at home and off oxygen, number of days 1-48;
  4: not hospitalized and either at home on oxygen or not home;
  5: hospitalized for medical care or in hospice care; and
  6: dead.
  If participant is censored, Cat = NA.
U: The time at which the outcome category was determined or the censoring time. For Cat = 1-5, U is the interim analysis time (90 days). For Cat = 6, U is the time of death. For Cat = NA, U is the censoring time.
delta: The event indicator (1 if U is the time at which the outcome category was determined; 0 if censored).
x: A continuous baseline covariate.
start: The lower bound of the time interval to which the given covariate values pertain.
stop: The upper bound of the time interval to which the given covariate values pertain.
hospStatus: A time-dependent indicator of hospital status, where 1 indicates that the participant was not in the hospital during interval [start, stop]; 0 otherwise.
daysOut: The expected number of continuous days out of hospital at the time of the interim analysis (90 days).
Estimation of the Odds Ratio in a Proportional Odds Model with Censored Time-lagged Outcome

Description

Inverse probability weighted complete case (IPWCC) and augmented inverse probability weighted complete case (AIPWCC) estimators for the odds ratio in a proportional odds model with time-lagged ordered categorical outcome in a randomized clinical trial.

Usage

tLagPropOdds(data, ..., ti = NULL, td = NULL, itmax = 500, tol = 1e-05)

Arguments

data: A data.frame object. A data.frame containing all observed data. At a minimum, this data.frame must contain columns with headers "id", "U", "delta", "Cat" and "A". If the time-independent component of the estimator is to be included, data.frame must also contain the bases of f(X). If the time-dependent component is included, data.frame must also contain the bases of h(X,L) as well as the time intervals with column headers {"tstart", "tstop"} or {"start","stop"}. See Details for additional information.

...: Ignored. Included to require named inputs.

ti: A character or integer vector or NULL. The columns of data to be included in the time-independent component of the estimator, f_m(X) m = 0, ..., M. If NULL, the time-independent component is excluded from the AIPWCC estimator. See Details for additional information.

td: A character or integer vector or NULL. The columns of data to be included in the time-dependent component of the estimator, h_l(X,Lbar), l = 1, ..., L. If NULL, the time-dependent component is excluded from the AIPWCC estimator. See Details for additional information.

itmax: An integer object. The maximum number of iterations for the Newton-Raphson algorithm used to estimate parameters alpha and beta.

tol: A numeric object. The value at which the Newton-Raphson is deemed to have converged.

Details

At a minimum, the data provided for the analysis must contain the following information:

id: A unique participant identifier.
U: The time to ascertainment of category or censoring.
delta: The indicator of ascertainment of category (1 if U is the time to ascertainment; 0 otherwise).
Cat: The ordered outcome category. Data must be provided as a factor or an integer or be able to be converted to an integer without loss of information. If participant was censored (delta = 0), Cat can take any integer-like value or NA.

A: The treatment received. Data must be provided as a factor or an integer or be able to be converted to an integer without loss of information.

With the exception of Cat, data must be complete.

If the time-independent component is to be included in the AIPWCC estimator, data must also include the time-independent basis functions f_m(X) m = 0, ..., M. If the intercept (f_0) term is not provided, it will be added by the software.

If the time-dependent component is to be included in the AIPWCC estimator, the data.frame must be a time-dependent dataset as described by package survival. Specifically, the time-dependent data must be specified for intervals [start,stop], and the data must include the following additional columns:

- **tstart:** The lower boundary of the time interval to which the data pertain.
- **tstop:** The upper boundary of the time interval to which the data pertain.

Note that column headers {"start", "stop"} are also accepted.

The various combinations of inputs ti and td yield the following:

- **ti = NULL, td = NULL** the IPWCC estimate is returned. (denoted as IPW in the simulations of the original manuscript.)
- **ti != NULL, td != NULL** the IPWCC and the full AIPWCC estimates are returned. (denoted as AIPW2 in the simulations of the original manuscript.)
- **ti = NULL, td != NULL** the IPWCC and the partial, time-independent AIPWCC estimates are returned. (denoted as AIPW1 in the simulations of the original manuscript.)
- **ti = NULL, td != NULL** the IPWCC and the partial, time-dependent AIPWCC estimates are returned. (not discussed in the simulations of the original manuscript.)

If a treatment subgroup has <5% censoring, a message is generated and the treatment subgroup is removed from the time-dependent component of the AIPWCC estimator. If there is no censoring, the IPWCC estimator approaches the usual proportional odds estimator.

**Value**

An S3 object of class tLagObj containing a list. The elements of the list correspond to the selected AIPWCC and/or IPWCC estimators. For each estimator, two matrix objects are returned: $logOdds contains the estimated beta parameters, their standard errors estimated using the sandwich estimator, the 95% confidence intervals, and the p-values for the log odds ratio; $odds contains the estimated odds ratio, their standard errors estimated using the delta method, and the 95% confidence intervals. The S3 object has an additional attribute, "type" giving a verbose description of the components contained in the estimator.
Examples

data(tLagData)

# full AIPWCC estimator
tLagPropOdds(data = tLagData, ti = "x", td = c("hospStatus", "daysOut"))

# partial, time-dependent AIPWCC estimator
tLagPropOdds(data = tLagData, td = c("hospStatus", "daysOut"))

# partial, time-independent AIPWCC estimator
tLagPropOdds(data = tLagData, ti = "x")
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