Package: multipleOutcomes (via r-universe)

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Title Joint Covariance and Treatment-Effect Tests for Multiple Outcomes

Version 0.18.1

Description Fits generalized linear models, Cox proportional-hazards models, log-rank tests, generalized estimating equations, mixed models with repeated measures, Kaplan-Meier curves, quantile differences, and hierarchical net-benefit (win-difference) and log win-ratio statistics jointly across multiple endpoints, and returns the full asymptotic covariance matrix linking them. Implements PATED (Prognostic Assisted Treatment Effect Detection), a randomized-trial method that exploits balanced prognostic covariates to tighten standard errors and increase statistical power without introducing bias.

URL https://github.com/zhangh12/multipleOutcomes, https://zhangh12.github.io/multipleOutcomes/

BugReports https://github.com/zhangh12/multipleOutcomes/issues

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Encoding UTF-8

Imports dplyr, ggplot2, ggpubr, mmrm (>= 0.3.15), mvtnorm, rlang, sandwich, stringr, survival, tidyr, tidyselect

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`actg` *ACTG 320 Clinical Trial Dataset*

Description

actg dataset from Hosmer et al.

Format

A data frame

id Identification Code

time Time to AIDS diagnosis or death (days).

censor Event indicator. 1 = AIDS defining diagnosis, 0 = Otherwise.

time_d Time to death (days)

censor_d Event indicator for death (only). 1 = Death, 0 = Otherwise.

tx Treatment indicator. 1 = Treatment includes IDV, 0 = Control group.

txgrp Treatment group indicator. 1 = ZDV + 3TC. 2 = ZDV + 3TC + IDV. 3 = d4T + 3TC. 4 = d4T + 3TC + IDV.

strat2 CD4 stratum at screening. 0 = CD4 <= 50. 1 = CD4 > 50.

sex 0 = Male. 1 = Female.

raceth Race/Ethnicity. 1 = White Non-Hispanic. 2 = Black Non-Hispanic. 3 = Hispanic. 4 = Asian, Pacific Islander. 5 = American Indian, Alaskan Native. 6 = Other/unknown.

ivdrug IV drug use history. 1 = Never. 2 = Currently. 3 = Previously.

hemophil Hemophiliac. 1 = Yes. 0 = No.

karnof Karnofsky Performance Scale. 100 = Normal; no complaint no evidence of disease. 90 = Normal activity possible; minor signs/symptoms of disease. 80 = Normal activity with effort; some signs/symptoms of disease. 70 = Cares for self; normal activity/active work not possible.

cd4 Baseline CD4 count (Cells/Milliliter).

priorzdv Months of prior ZDV use (months).

age Age at Enrollment (years).

Source

ftp://ftp.wiley.com/public/sci_tech_med/survival

References

Hosmer, D.W. and Lemeshow, S. and May, S. (2008) Applied Survival Analysis: Regression Modeling of Time to Event Data: Second Edition, John Wiley and Sons Inc., New York, NY

Examples

```
data(actg)
```

---

coef.jointCovariance *Extract Model Coefficients*

Description

`coef` is a generic function.

Usage

```
## S3 method for class 'jointCovariance'
coef(object, model_index = NULL, ...)
```

Arguments

object	an object returned by jointCovariance().
model_index	NULL if displaying coefficients of all fitted models; otherwise, an integer indicating the fitted model.
...	for debugging only

Value

a vector of coefficient estimates

---

coxph_ *Creating Objects of Proportional Hazards Regression Model*

Description

coxph_ is a wrapper function of survival::coxph to create an object to be passed into jointCovariance, the main function of this package through its argument .... The object defines how a proportional hazard model would be fitted.

Usage

```
coxph_(formula, data_index = 1)
```

Arguments

formula	see formula in survival::coxph.
data_index	integer. Index of the data frame in the data argument of jointCovariance to be used when fitting a proportional hazards model.

Details

Not all arguments of survival::coxph are supported in coxph_ due to the complexity in handling environment and scope, which is particularly difficult for arguments like weights, subset, etc.

gee_ *Creating Objects of Generalized Estimation Equation Model*

Description

gee_ is a wrapper function of gee::gee to create an object to be passed into jointCovariance, the main function of this package through its argument .... The object defines how a GEE model would be fitted.

This package does not import the package gee. Instead, codes of gee are modified and integrated to compute score and information matrix. Thus, users does not need to install the package gee to use this package.

Usage

```
gee_(formula, family, corstr, R = NULL, b = NULL, Mv = 1, data_index = 1)
```

Arguments

formula	see formula in gee::gee.
family	see family in gee::gee.
corstr	see corstr in gee::gee.
R	see R in gee::gee.
b	see b in gee::gee.
Mv	see Mv in gee::gee.
data_index	integer. Index of the data frame in the data argument of jointCovariance to be used when fitting a GEE model.

Details

Not all arguments of stats::gee are supported in gee_ due to the complexity in handling environment and scope, which is particularly difficult for arguments like subset, etc.

glm_ *Creating Objects of Generalized Linear Models*

Description

glm_ is a wrapper function of stats::glm to create an object to be passed into jointCovariance, the main function of this package through its argument .... The object defines how a GLM model would be fitted.

Usage

```
glm_(formula, family, data_index = 1)
```

Arguments

formula	see formula in stats::glm.
family	currently supports "gaussian" or "binomial". Other families are under testing.
data_index	integer. Index of the data frame in the data argument of jointCovariance to be used when fitting a generalized linear model.

Details

Not all arguments of stats::glm are supported in glm_ due to the complexity in handling environment and scope, which is particularly difficult for arguments like weights, subset, etc.

---

indo *Rectal Indomethacin for Prevention of Post-ERCP Pancreatitis*

Description

Patient-level data from a multi-center, randomized, double-blind, placebo-controlled 2-arm trial (n = 602) of rectal indomethacin (100 mg) versus placebo to prevent post-ERCP pancreatitis in high-risk patients, as reported by Elmunzer, Higgins, et al. (2012) in the *New England Journal of Medicine*.

This dataset was originally collected, cleaned, reformatted, and released for public teaching and research use by Dr. Peter D. R. Higgins in the **medicaldata** R package as indo_rct. The version shipped here is redistributed in support of the worked examples in this package. The variable definitions below follow **medicaldata**; note that a few columns are stored as numeric (rather than factor) in this copy. Users who need the authoritative copy or accompanying documentation should consult **medicaldata**.

Format

A data frame with 602 observations on the following 33 variables:

id Subject identifier (numeric); leading digit indicates center. Range 1001–4003.

site Study site (factor, 4 levels): 1_UM = University of Michigan, 2_IU = Indiana University, 3_UK = University of Kentucky, 4_Case = Case Western Reserve University.

age Age in years (numeric), range 19–90.

risk Risk score for post-ERCP pancreatitis (numeric), range 1–5.5.

gender Sex (factor): 1_female, 2_male.

outcome Primary outcome: post-ERCP pancreatitis (numeric, 1 = yes, 0 = no).

sod Sphincter of Oddi dysfunction present (factor): 0_no, 1_yes.

pep History of prior post-ERCP pancreatitis (factor): 0_no, 1_yes.

recpanc History of recurrent pancreatitis (factor): 0_no, 1_yes.

psphinc Pancreatic sphincterotomy performed (factor): 0_no, 1_yes.

`precut` Sphincter pre-cut needed to enter papilla (factor): `0_no`, `1_yes`.

`difcan` Cannulation of papilla was difficult (factor): `0_no`, `1_yes`.

`pneudil` Pneumatic dilation of papilla performed (factor): `0_no`, `1_yes`.

`amp` Ampullectomy performed (factor): `0_no`, `1_yes`.

`paninj` Contrast injected into pancreas (factor): `0_no`, `1_yes`.

`acinar` Pancreas appeared to have acinarization on imaging (factor): `0_no`, `1_yes`.

`brush` Brushings taken from pancreatic duct (factor): `0_no`, `1_yes`.

`asa81` Aspirin used at 81 mg per day (factor with 3 levels): `0_no`, `1_yes`, and a third level retained from the source coding.

`asa325` Aspirin used at 325 mg per day (factor with 3 levels): `0_no`, `1_yes`, and a third level retained from the source coding.

`asa` Aspirin used at any dose (factor with 3 levels): `0_no`, `1_yes`, and a third level retained from the source coding.

`prophystent` Pancreatic duct stent placed per endoscopist judgment (factor): `0_no`, `1_yes`.

`therastent` Pancreatic duct stent placed to treat narrowing (factor): `0_no`, `1_yes`.

`pdstent` Pancreatic duct stent placed for any reason (factor): `0_no`, `1_yes`.

`sodsom` Sphincter of Oddi manometry performed (factor): `0_no`, `1_yes`.

`bsphinc` Biliary sphincterotomy performed (factor): `0_no`, `1_yes`.

`bstent` Biliary stent placed to relieve obstruction (factor): `0_no`, `1_yes`.

`chole` Choledocholithiasis present (factor): `0_no`, `1_yes`.

`pbmal` Biliary duct or pancreatic malignancy found (factor): `0_no`, `1_yes`.

`train` Trainee participated in ERCP (factor): `0_no`, `1_yes`.

`status` Patient status (factor): `0_inpatient`, `1_outpatient`.

`type` Sphincter of Oddi dysfunction type (factor): `0_no SOD`, `1_type 1`, `2_type 2`, `3_type 3`.

`rx` Treatment assignment (numeric, 1 = indomethacin, 0 = placebo).

`bleed` Reportable gastrointestinal bleeding (numeric, coded 1 = no, 2 = yes; `NA` when not assessed).

Source

Higgins, P. D. R. **medicaldata**: Data Package for Medical Datasets. R package, dataset `indo_rct`. https://CRAN.R-project.org/package=medicaldata

References

Elmunzer BJ, Higgins PDR, Saini SD, et al. A randomized trial of rectal indomethacin to prevent post-ERCP pancreatitis. *New England Journal of Medicine* 2012; 366(15):1414–1422. doi:10.1056/NEJMoa1111103

Examples

```
data(indo)
```

`jointCovariance` *Fitting Regression Models for Multiple Outcomes and Returning the Matrix of Covariance*

Description

`jointCovariance` can fit different types of models for multiple outcomes simultaneously and return model parameters and variance-covariance matrix for further analysis.

Usage

```
jointCovariance(..., data, nboot = 0, compute_cov = TRUE, seed = NULL)
```

Arguments

`...`	objects returned by `glm_()`, `coxph_()`, `logrank_()`, `gee_()`, `mmrm_()`, `km_()`, `quantile_()`, `netbenefit_()`, or `winratio_()`.
`data`	a data frame if all models are fitted on the same dataset; otherwise a list of data frames for fitting models in `...`. Note that a dataset can be used to fit multiple models, thus, `length(data)` is unnecessary to be equal to the number of models in `...`. The row names in a data frame are not treated as subject IDs. Instead, all data frame should consist of a column `pid` as subject IDs. For any two records in different data frames that correspond to the same subject, their values in `pid` should be consistent. For data frames to be used by GEE, `pid` defines clusters. See `id` and the Details section of `gee:gee`.
`nboot`	non-zero integer if bootstrap is adopted. By default 0.
`compute_cov`	logic. If `TRUE` and `nboot > 0`, empirical covariance matrix is computed using bootstrap estimate and returned. Bootstrap estimate will be abandoned. If `FALSE`, bootstrap estimate will be returned and no empirical covariance matrix is computed.
`seed`	random seed when generate bootstrap data.

Value

It returns an object of class "jointCovariance", which is a list containing the following components:

`coefficients`	an unnamed vector of coefficients of all fitted models. Use `id_map` for variable mapping.
`mcov`	a unnamed matrix of covariance of `coefficients`. Use `id_map` for variable mapping.
`id_map`	a list mapping the elements in `coefficients` and `mcov` to variable names.
`n_shared_sample_sizes`	a matrix of shared sample sizes between datasets being used to fit the models.
`call`	the matched call.

Examples

```
## More examples can be found in the vignettes.
library(survival)
library(mvtnorm)
library(tidyr)
genData <- function(seed = NULL){

  set.seed(seed)
  n <- 300
  sigma <- matrix(.7, 4, 4)
  diag(sigma) <- 1
  v <- rmvnorm(n, sigma = sigma)
  x1 <- v[, 1]
  x2 <- v[, 2]
  z1 <- (v[, 3] > 0) + 0
  z2 <- v[, 4]

  trt <- rbinom(n, 1, .5)

  bet <- c(-.3,.3)
  y <- -log(runif(n))/
    exp(-.3 * x1 + .3 * x2 + z1 * .5 - z2 * .3 + .1 * trt + rnorm(n))

  z1[sample.int(n, 50)] <- NA
  z2[sample.int(n, 50)] <- NA
  x1[sample.int(n, 50)] <- NA
  x2[sample.int(n, 50)] <- NA
  death <- ifelse(y > 2, 0, 1)
  y[y > 2] <- 2

  pid <- paste0('pid-', 1:n)
  ret <- data.frame(
    y = y, trt = trt,
    z1 = z1, z2 = z2,
    x1 = x1, x2 = x2,
    death, pid)
  ret
}

dat1 <- genData()

## create a dataset with repeated measurements x
dat2 <- dat1 %>% pivot_longer(c(x1, x2), names_to='visit', values_to='x') %>%
  dplyr::select(x, trt, visit, pid) %>% as.data.frame()

dat2$visit <- as.factor(dat2$visit)
dat2$pid <- as.factor(dat2$pid)

fit <- jointCovariance(
  coxph_(Surv(time = y, event = death) ~ trt, data_index = 1),
  logrank_(Surv(time = y, event=death) ~ trt, data_index = 1),
  glm_(z1 ~ trt, family = 'binomial', data_index = 1),
```

```
  glm_(z2 ~ trt, family = 'gaussian', data_index = 1),
  mmrm_(x ~ trt + us(visit | pid), reml = TRUE, data_index = 2),
  gee_(x ~ trt, family = 'gaussian', corstr = 'independence', data_index = 2),
  data = list(dat1, dat2))

fit


bfit <-jointCovariance(
  coxph_(Surv(time=y, event=death) ~ trt, data_index = 1),
  logrank_(Surv(time=y, event=death) ~ trt, data_index = 1),
  glm_(z1 ~ trt, family = 'binomial', data_index = 1),
  glm_(z2 ~ trt, family = 'gaussian', data_index = 1),
  mmrm_(x ~ trt + us(visit | pid), reml = TRUE, data_index = 2),
  gee_(x ~ trt, family = 'gaussian', corstr = 'independence', data_index = 2),
  data = list(dat1, dat2), nboot = 10)

summary(bfit)

## km_() and quantile_() require nboot > 0 because they have no
## closed-form score. compute_cov is forced to FALSE for km_().
## When all models share one dataset, `data_index` and `list(...)`
## can be omitted.
kfit <- jointCovariance(
  km_(Surv(time = y, event = death) ~ trt, conf_type = 'log',
      times = c(0.5, 1, 1.5)),
  glm_(z1 ~ trt, family = 'binomial'),
  data = dat1, nboot = 30, seed = 1)

qfit <- jointCovariance(
  quantile_(y ~ trt, probs = c(0.25, 0.5, 0.75)),
  glm_(z2 ~ trt, family = 'gaussian'),
  data = dat1, nboot = 30, seed = 1)
```

---

km_ *Creating Objects of Kaplan-Meier Curve*

Description

km_ is a wrapper function creating an object of Kaplan-Meier curve to be passed into `jointCovariance`, the main function of this package through its argument . . . . The object defines how a Kaplan-Meier curve would be fitted.

Usage

```
km_(formula, times = NULL, conf_type, data_index = 1)
```

Arguments

formula	a formula created by survival::Surv().
times	numeric vector of time. Survival probabilities at times are computed (with g-transformation defined by conf_type).
conf_type	character. Type of confidence interval. It must be one of "log", "log-log", "plain", "logit", or "arcsin".
data_index	integer. Index of the data frame in the data argument of jointCovariance to be used when fitting a generalized linear model.

Details

Usually, g-transformation is applied to the survival probability S(t) to obtain pointwise confidence interval of a Kaplan-Meier curve. This can be achieved by specifying conf_type. For identity transformation, use conf_type = "plain".

This function can only be used with jointCovariance when the bootstrap method is used to estimate variance-covariance matrix of multiple outcome models.

---

logrank_ *Creating Objects of Logrank Test*

Description

logrank_ is a wrapper function survival::coxph to create an object to be passed into jointCovariance, the main function of this package through its argument .... Logrank test is the score test under the proportional hazards regression model. The object defines how a logrank test would be computed.

Usage

```
logrank_(formula, ties = c("efron", "breslow", "exact"), data_index = 1)
```

Arguments

formula	see formula in survival::coxph.
ties	character string specifying the method for tie handling. One of "efron" (default), "breslow", or "exact". Passed through to survival::coxph.
data_index	integer. Index of the data frame in the data argument of jointCovariance to be used when computing testing statistic of logrank test.

Details

Not all arguments of survival::coxph are supported in logrank_ due to the complexity in handling environment and scope, which is particularly difficult for arguments like weights, subset, etc.

mmrm_ *Creating Objects of Mixed Models for Repeated Measures*

Description

mmrm_ is a wrapper function of mmrm::mmrm to create an object to be passed into jointCovariance, the main function of this package through its argument .... The object defines how a MMRM model would be fitted.

Usage

```
mmrm_(
  formula,
  covariance = NULL,
  reml = TRUE,
  control = mmrm::mmrm_control(...),
  ...,
  data_index = 1
)
```

Arguments

formula	see formula in mmrm::mmrm.
covariance	see covariance in mmrm::mmrm.
reml	see reml in mmrm::mmrm.
control	see control in mmrm::mmrm.
...	see ... in mmrm::mmrm.
data_index	integer. Index of the data frame in the data argument of jointCovariance to be used when fitting a GEE model.

Details

The argument weights of mmrm::mmrm is supported in mmrm_ due to the complexity in handling environment and scope.

Please always refer to help document of mmrm::mmrm before using mmrm_. For example, time variable and observation ID must be factor variables in some cases, otherwise error may be prompted. Users can call mmrm::mmrm using the same arguments being passed to mmrm_ to check validity.

nb_endpoint *Endpoint Constructors for netbenefit_()*

Description

These helpers build the individual endpoint specifications that `netbenefit_()` consumes through its `endpoints` argument. Each call returns a small list describing one comparison rule; the order in which they appear in the `endpoints` list defines the hierarchical priority (first = highest).

Usage

```
nb_tte(
  time,
  event,
  direction = c("longer_better", "shorter_better"),
  margin = 0,
  censor_rule = c("informative", "ignore")
)

nb_continuous(
  value,
  direction = c("larger_better", "smaller_better"),
  margin = 0
)

nb_binary(value, direction = c("larger_better", "smaller_better"))
```

Arguments

`time`	character. Name of the time column in `data`.
`event`	character. Name of the event-indicator column in `data` (1 = event observed, 0 = censored).
`direction`	one of `"longer_better"` / `"shorter_better"` (`nb_tte()`) or `"larger_better"` / `"smaller_better"` (`nb_continuous()`, `nb_binary()`).
`margin`	non-negative numeric. Minimum directional gap required to declare a winner on this endpoint. Defaults to 0.
`censor_rule`	(`nb_tte()` only) one of `"informative"` / `"ignore"`.
`value`	character. Name of the outcome column in `data`.

Value

An object of class `c("nb_endpoint_<type>", "nb_endpoint")` carrying the rule and its arguments.

Direction

For each endpoint type, `direction` says whether a larger value (or longer time, for TTE) counts as a win for the subject. With the default convention, a treatment subject "wins" the endpoint when its value, possibly minus a margin, exceeds the control subject's value. Flip the default for endpoints where smaller (or shorter) is better (e.g., pain scores; time to symptom relief).

Margin

`margin` is a non-negative clinically meaningful difference threshold. A pair only declares a winner when the directional gap strictly exceeds `margin`; otherwise the pair ties at this endpoint and falls through to the next one. `nb_binary()` does not expose `margin` because binary values admit only two outcomes.

Censoring

`nb_tte()` accepts a `censor_rule` argument. The default `"informative"` matches the conventional Pocock/Buyse rule: if one subject is censored and the other observed, a winner can only be declared in the direction the censoring is uninformative about (i.e., the censored time is already past the event time). `"ignore"` drops pairs where either subject is censored and treats them as ties at this level.

See Also

`netbenefit_()`

---

netbenefit_ *Creating Objects of Hierarchical Net-Benefit (Win-Difference) Statistic*

Description

`netbenefit_` creates an object to be passed into `jointCovariance` or `pated` through its `...` argument. The object defines a hierarchical net-benefit (a.k.a. win-difference, proportion-in-favor) statistic across a list of endpoints, each declared by `nb_tte()`, `nb_continuous()`, or `nb_binary()`.

Usage

```
netbenefit_(formula, endpoints, data_index = 1)
```

Arguments

`formula`	a two-sided R formula `<label> ~ arm`. The LHS is used purely as a row label in `pated()` output; the RHS must contain exactly one variable, the column in `data` holding treatment-arm assignment.
`endpoints`	a non-empty list of endpoint specs built by `nb_tte()`, `nb_continuous()`, or `nb_binary()`. The order of the list encodes the hierarchical priority: endpoint 1 is checked first; if it ties, the pair falls through to endpoint 2; and so on.
`data_index`	integer. Index of the data frame in the `data` argument of `jointCovariance` to be used.

Details

The estimator is

$$\widehat{\Delta} = \frac{N_W - N_L}{N_W + N_L + N_T}$$

where N_W, N_L, and N_T are the numbers of treatment wins, losses, and overall ties across all $n_C \times n_T$ pairs (control vs. treatment subject). The per-subject influence function is available in closed form, so both the asymptotic and the bootstrap paths of `jointCovariance` are supported.

The arm reference level is inferred from the arm column the same way `model.matrix(~ arm)` would: `levels(arm)[1]` for factor, the smaller value for numeric or logical, and the alphabetically first value for character. To override, convert the column to a factor with the desired level order before calling `netbenefit_()`.

Value

An object of class `c("jc_spec_netbenefit", "jc_spec")`.

See Also

`nb_tte()`, `nb_continuous()`, `nb_binary()`, `jointCovariance()`, `pated()`.

---

oak *OAK Phase III Trial of Atezolizumab vs Docetaxel in NSCLC*

Description

Patient-level data (primary intention-to-treat population, n = 850) from OAK, an international, open-label, randomized Phase III trial (NCT02008227) comparing the anti-PD-L1 antibody atezolizumab (MPDL3280A, 1200 mg IV every 3 weeks) with docetaxel (75 mg/m^2 IV every 3 weeks) as second- or third-line therapy in patients with previously treated locally advanced or metastatic non-small-cell lung cancer (NSCLC). Patients were randomized 1:1 to the two arms.

The variables retained here are those released in Supplementary Table 8 of Gandara et al. (2018), *Nature Medicine*, who retrospectively assayed banked baseline plasma samples for blood-based tumor mutational burden (bTMB) and reported the biomarker-evaluable analyses on this primary ITT cohort. The shipped copy applies the following purely cosmetic transformations to the source: source variable names lower-cased; categorical values lower-cased; the string `"."` (the source's missing code) converted to `NA`; numeric-looking character columns coerced to numeric; and the event indicators inverted so that `1 = event, 0 = censored` (the source uses the opposite convention). Categorical variables are stored as **character** vectors (not factors); convert to factor on demand with `factor()` if a modeling function requires it. No rows are dropped: the full primary ITT population is included.

Authoritative reference. This documentation is a convenience summary; users should consult the original publication and its supplementary materials (Gandara et al. 2018; Rittmeyer et al. 2017) for the definitive description of the trial design, eligibility criteria, endpoint definitions, and assay protocol.

Format

A data frame with 850 observations on 27 variables:

`id` Anonymized patient identifier; integer 301–1150. *(identifier)*

`arm` Randomized treatment assignment, character: `"docetaxel"` or `"atezolizumab"`. *(treatment assignment)*

`pfs` Progression-free survival, months (numeric). *(post-randomization outcome)*

`pfs_event` PFS event indicator, integer: 1 = progression or death, 0 = censored. Inverted from the source's `PFS.CNSR`. *(post-randomization outcome)*

`os` Overall survival, months (numeric). *(post-randomization outcome)*

`os_event` OS event indicator, integer: 1 = death, 0 = censored. Inverted from the source's `OS.CNSR`. *(post-randomization outcome)*

`bcor` Best confirmed overall response per investigator (RECIST 1.1), character: `"CR"`, `"PR"`, `"SD"`, `"PD"`, `"NE"`; `NA` when not assessable. *(post-randomization outcome)*

`btmb` Blood-based tumor mutational burden: count of somatic base substitutions on a 394-gene, $\sim$1.1 Mb panel of cell-free DNA from the baseline plasma sample (numeric); `NA` when the assay was not run or failed QC. *(baseline characteristic; predictive of atezolizumab benefit at $btmb \geq 16$; not strongly prognostic in itself)*

`msaf` Maximum somatic allele frequency in the baseline cfDNA sample (numeric, 0–1); a tumor-content / shedding surrogate. *(baseline characteristic; weakly prognostic)*

`cfdna_ng` cfDNA mass entering NGS library construction (nanograms, numeric, capped at 100 ng). *(baseline characteristic; not prognostic — assay input)*

`coverage` Median exon sequencing coverage (numeric). *(baseline characteristic; not prognostic — assay quality)*

`qc` bTMB assay QC status, character: `"pass"`, `"fail"`; `NA` when not run. *(baseline characteristic; not prognostic — assay quality)*

`bep` Logical flag for the biomarker-evaluable population used in the bTMB analyses: `coverage >= 800 & qc == "pass" & msaf >= 0.01` (n = 642 of 850). *(baseline derived flag; not prognostic in itself)*

`age` Baseline age, years (numeric); range 33–85. *(baseline characteristic; modestly prognostic)*

`sex` Sex, character: `"F"`, `"M"`. *(baseline characteristic; weakly prognostic; correlates with smoking and bTMB)*

`race` Race, character: `"white"`, `"asian"`, `"other"`. *(baseline characteristic; not robustly prognostic in this setting)*

`histology` Tumor histology, character: `"non-squamous"`, `"squamous"`. *(baseline characteristic; modestly prognostic)*

`ecog` ECOG performance status at baseline, integer (0 or 1). *(baseline characteristic; strongly prognostic for PFS and OS)*

`prior_tx` Number of prior lines of systemic therapy, integer (1 or 2). *(baseline characteristic; prognostic — patients with 2 prior lines tend to do worse)*

`smoking` Smoking history, character: `"never"`, `"previous"`, `"current"`. *(baseline characteristic; modestly prognostic and also a correlate of IO benefit through bTMB)*

`sld` Baseline sum of longest diameters of target lesions per RECIST 1.1, mm (numeric). *(baseline characteristic; strongly prognostic — tumor burden)*

`metsites` Number of metastatic sites at enrollment, integer. *(baseline characteristic; strongly prognostic — disease burden)*

`kras` *KRAS* mutation status from CRF, character: `"negative"`, `"positive"`; `NA` when not tested. *(baseline characteristic; weakly / inconsistently prognostic; possible predictive signal for IO)*

`egfr` *EGFR* mutation status from CRF, character: `"negative"`, `"positive"`; `NA` when not tested. *(baseline characteristic; weakly prognostic in IO-treated populations; strongly predictive of differential treatment effect — EGFR-positive patients typically derive less benefit from anti-PD-L1)*

`eml4` *EML4-ALK* rearrangement status from CRF, character: `"negative"`, `"positive"`; `NA` when not tested. *(baseline characteristic; analogous to* `egfr` *in interpretation — predictive of reduced IO benefit)*

`tc1ic1` PD-L1 IHC (Ventana SP142) dichotomized at the TC1IC1 cut-point, character: `"low"` = `TC0` and `IC0`; `"high"` = `TC1/2/3` or `IC1/2/3`; `NA` when unknown. *(baseline characteristic; predictive of atezolizumab benefit; weakly prognostic)*

`tc3ic3` PD-L1 IHC dichotomized at the TC3IC3 cut-point, character: `"low"` = `TC0/1/2` and `IC0/1/2`; `"high"` = `TC3` or `IC3`; `NA` when unknown. *(baseline characteristic; predictive of atezolizumab benefit; weakly prognostic)*

Details

OAK's trial-level eligibility criteria (locally advanced or metastatic NSCLC after platinum failure, ECOG 0–1, measurable disease per RECIST 1.1, no prior immune-checkpoint therapy, adequate organ function, etc.) were applied **before** randomization, so the n = 850 primary ITT cohort is randomized 1:1. The bTMB assay was performed retrospectively on banked baseline plasma; all assay-derived variables therefore reflect quantities present before treatment exposure but were generated post-randomization in calendar time. *EGFR*, *EML4-ALK*, and PD-L1 IHC are recorded at screening and can be used to subset without compromising randomization. The published bTMB analyses (PFS and OS hazard ratios at the `btmb >= 16` cut-point) used the subset `bep & !(egfr %in% "positive") & !(eml4 %in% "positive")` (n = 583). OAK published a primary ITT of 850 patients and a secondary ITT of 1225 patients; only the primary ITT is included here. Variant-level information (per-mutation chromosome, position, gene, protein change, etc.) was released alongside this table but is not included here.

Variable role labels

Each variable in the format section above carries a role tag in italic parentheses at the end of its description. The tags combine two dimensions:

- **Baseline characteristic** — measured (or, for the bTMB assay, derived from material collected) at the baseline visit before the first dose of study treatment. Using such variables as covariates does not break randomization in expectation, because they are functions of pre-treatment quantities only.
- **Prognostic** — based on the clinical-oncology literature for previously treated advanced NSCLC, whether the variable has been reported to be associated with PFS or OS independent of treatment assignment. "Predictive" indicates association with differential atezolizumab vs docetaxel benefit rather than with outcome per se. Strength qualifiers (strong / modest / weak) are

the author's reading of the literature and are no substitute for a formal analysis on the dataset at hand.

Variables that are outcomes, identifiers, or treatment assignment carry a single role tag in place of the two-dimensional tag.

Pre- vs post-randomization variables

For users planning to apply PATED or any analysis that relies on baseline covariates being balanced across arms:

Pre-randomization (collected at screening; safe to condition on): `age`, `sex`, `race`, `histology`, `ecog`, `prior_tx`, `smoking`, `sld`, `metsites`, `kras`, `egfr`, `eml4`, `tc1ic1`, `tc3ic3`.

Pre-treatment but derived post-randomization (measured on the baseline blood draw, before first dose; empirically b `btmb`, `msaf`, `cfdna_ng`, `coverage`, `qc`, `bep`.

Post-randomization outcomes (must not be used as covariates): `pfs`, `pfs_event`, `os`, `os_event`, `bcor`.

Conditioning on the biomarker-evaluable population (`bep == TRUE`, n = 642) or further restricting to `!(egfr %in% "positive") & !(eml4 %in% "positive")` (the paper's primary bTMB analysis subgroup, n = 583) is a selection on pre-treatment variables and does not break randomization in expectation; Supp. Tables 4 and 5 of the source paper confirm empirical arm-balance (no nominally significant imbalance on age, race, ECOG, histology, prior lines, *KRAS*, or PD-L1 IHC; the `btmb >= 16` subgroup is enriched for males and for smokers, but those are biomarker–covariate associations, not arm–covariate associations). Users should still verify arm-balance on their working subset (e.g. with **tableone**) before invoking methods that assume it.

Source

Built from Supplementary Table 8 (Excel file MOESM3) of: Gandara DR, Paul SM, Kowanetz M, Schleifman E, Zou W, Li Y, Rittmeyer A, Fehrenbacher L, Otto G, Malboeuf C, Lieber DS, Lipson D, Silterra J, Amler L, Riehl T, Cummings CA, Hegde PS, Sandler A, Ballinger M, Fabrizio D, Mok T, Shames DS. Blood-based tumor mutational burden as a predictor of clinical benefit in non-small-cell lung cancer patients treated with atezolizumab. *Nature Medicine* 2018; 24(9):1441–1448. doi:10.1038/s41591018013343. Supplementary file downloaded from https://www.nature.com/articles/s41591-018-0134-3. See `data-raw/poplar_oak.R` in the package source for the exact cleaning steps. Redistribution in this package is for non-commercial research and teaching use; users intending other use should verify the licensing terms of the Springer Nature supplementary materials. **Always cite the original publication when using this dataset.**

References

Rittmeyer A, Barlesi F, Waterkamp D, Park K, Ciardiello F, von Pawel J, Gadgeel SM, Hida T, Kowalski DM, Dols MC, Cortinovis DL, Leach J, Polikoff J, Barrios C, Kabbinavar F, Frontera OA, De Marinis F, Turna H, Lee JS, Ballinger M, Kowanetz M, He P, Chen DS, Sandler A, Gandara DR; OAK Study Group. Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a Phase 3, open-label, multicentre randomised controlled trial. *Lancet* 2017; 389(10066):255–265. doi:10.1016/S01406736(16)32517X.

Examples

```
data(oak)
table(oak$arm, useNA = "ifany")
summary(oak$btmb)
# Primary bTMB analysis subset (paper's n = 583); %in% keeps NA rows
# (untested patients) since they are not confirmed positive.
oak_bep <- subset(oak, bep & !(egfr %in% "positive") & !(eml4 %in% "positive"))
```

`pated` *Prognostic Variables Assisted Treatment Effect Detection*

Description

`pated` is a wrapper function of `jointCovariance` for testing treatment effect in randomized clinical trials. It assumes that prognostic variables are fully randomized. This assumption can help enhancing statistical power of conventional approaches in detecting the treatment effect. Specifically, the sensitivity of the conventional models specified in `...` are improved by `pated`.

Usage

```
pated(
  ...,
  data,
  nboot = 0,
  compute_cov = TRUE,
  seed = NULL,
  transform = "identity"
)
```

Arguments

`...`	model specifications built by `glm_()`, `coxph_()`, `logrank_()`, `gee_()`, `mmrm_()`, `km_()`, `quantile_()`, `netbenefit_()`, or `winratio_()`. The first specification is the primary outcome whose treatment effect is being tested; the rest are prognostic covariates used to tighten the SE.
`data`	either a single data frame (when all models are fitted on the same dataset) or a list of data frames (one entry per `data_index`). Each data frame must have a `pid` column carrying subject identifiers; records with the same `pid` across different data frames refer to the same subject.
`nboot`	non-zero integer if bootstrap is adopted. By default 0.
`compute_cov`	logic. If `TRUE`, empirical covariance matrix is computed using bootstrap estimate and returned. Bootstrap estimate will be abandoned. If `FALSE`, bootstrap estimate will be returned and no empirical covariance matrix is computed.
`seed`	random seed when generate bootstrap data.
`transform`	character. Now only supports `"identity"`.

Value

a data frame of testing results.

Examples

```
## More examples can be found in the vignettes.
library(survival)
library(mvtnorm)

genData <- function(seed = NULL){
  set.seed(seed)
  n <- 300
  sigma <- matrix(c(1, .6, .6, 1), 2)
  x <- rmvnorm(n, sigma = sigma)
  z1 <- rbinom(n, 1, .6)
  z2 <- rnorm(n)
  trt <- rbinom(n, 1, .5)

  bet <- c(-.2, .2)
  y <- -.5 + x %*% bet + z1 * .3 - z2 * .1 + .1 * trt - .1 * rnorm(n)
  death <- rbinom(n, 1, .8)
  data.frame(
    y = as.numeric(y), trt = trt,
    z1 = z1, z2 = z2,
    x1 = x[, 1], x2 = x[, 2],
    death, pid = paste0('s-', seq_len(n))
  )
}

dat <- genData(seed = 31415926)

## `data_index` defaults to 1 in every spec constructor and a single
## data.frame is auto-wrapped into a list, so neither needs spelling out
## when all models are fitted on the same dataset.
fit <-
  pated(
    coxph_(Surv(time = y, event = death) ~ trt),
    glm_(z1 ~ trt, family = 'binomial'),
    glm_(z2 ~ trt, family = 'gaussian'),
    glm_(x1 ~ trt, family = 'gaussian'),
    glm_(x2 ~ trt, family = 'gaussian'),
    data = dat
  )

fit
```

`plot.pated` *Plot PATED Analysis Results*

Description

Plot PATED Analysis Results

Usage

```
## S3 method for class 'pated'
plot(x, ...)
```

Arguments

x	an object returned from `pated()`.
...	currently not supported.

Value

`NULL`

`poplar` *POPLAR Phase II Trial of Atezolizumab vs Docetaxel in NSCLC*

Description

Patient-level data (full intention-to-treat population, n = 287) from POPLAR, a multi-center, open-label, randomized Phase II trial (NCT01903993) comparing the anti-PD-L1 antibody atezolizumab (MPDL3280A, 1200 mg IV every 3 weeks) with docetaxel (75 mg/m^2 IV every 3 weeks) as second- or third-line therapy in patients with previously treated locally advanced or metastatic non-small-cell lung cancer (NSCLC). Patients were randomized 1:1 to the two arms.

The variables retained here are those released in Supplementary Table 8 of Gandara et al. (2018), *Nature Medicine*, who retrospectively assayed banked baseline plasma samples for blood-based tumor mutational burden (bTMB). The shipped copy applies the following purely cosmetic transformations to the source: source variable names lower-cased; categorical values lower-cased; the string `"."` (the source's missing code) converted to `NA`; numeric-looking character columns coerced to numeric; and the event indicators inverted so that `1 = event, 0 = censored` (the source uses the opposite convention). Categorical variables are stored as **character** vectors (not factors); convert to factor on demand with `factor()` if a modeling function requires it. No rows are dropped: the full ITT population is included.

Authoritative reference. This documentation is a convenience summary; users should consult the original publication and its supplementary materials (Gandara et al. 2018; Fehrenbacher et al. 2016) for the definitive description of the trial design, eligibility criteria, endpoint definitions, and assay protocol.

Format

A data frame with 287 observations on 25 variables:

`id` Anonymized patient identifier; integer 1–287. *(identifier)*

`arm` Randomized treatment assignment, character: `"docetaxel"` or `"atezolizumab"`. *(treatment assignment)*

`pfs` Progression-free survival, months (numeric). *(post-randomization outcome)*

`pfs_event` PFS event indicator, integer: 1 = progression or death, 0 = censored. Inverted from the source's `PFS.CNSR`. *(post-randomization outcome)*

`os` Overall survival, months (numeric). *(post-randomization outcome)*

`os_event` OS event indicator, integer: 1 = death, 0 = censored. Inverted from the source's `OS.CNSR`. *(post-randomization outcome)*

`bcor` Best confirmed overall response per investigator (RECIST 1.1), character: `"CR"`, `"PR"`, `"SD"`, `"PD"`, `"NE"`; `NA` when not assessable. *(post-randomization outcome)*

`btmb` Blood-based tumor mutational burden: count of somatic base substitutions on a 394-gene, $\sim$1.1 Mb panel of cell-free DNA from the baseline plasma sample (numeric); `NA` when the assay was not run or failed QC. *(baseline characteristic; predictive of atezolizumab benefit at $btmb \geq 16$; not strongly prognostic in itself)*

`msaf` Maximum somatic allele frequency in the baseline cfDNA sample (numeric, 0–1); a tumor-content / shedding surrogate. *(baseline characteristic; weakly prognostic)*

`cfdna_ng` cfDNA mass entering NGS library construction (nanograms, numeric, capped at 100 ng). *(baseline characteristic; not prognostic — assay input)*

`coverage` Median exon sequencing coverage (numeric). *(baseline characteristic; not prognostic — assay quality)*

`qc` bTMB assay QC status, character: `"pass"`, `"fail"`; `NA` when not run. *(baseline characteristic; not prognostic — assay quality)*

`bep` Logical flag for the biomarker-evaluable population used in the bTMB analyses: `coverage >= 800 & qc == "pass" & msaf >= 0.01` (n = 211 of 287). *(baseline derived flag; not prognostic in itself)*

`age` Baseline age, years (numeric); range 36–84. *(baseline characteristic; modestly prognostic)*

`sex` Sex, character: `"F"`, `"M"`. *(baseline characteristic; weakly prognostic; correlates with smoking and bTMB)*

`race` Race, character: `"white"`, `"asian"`, `"other"`. *(baseline characteristic; not robustly prognostic in this setting)*

`histology` Tumor histology, character: `"non-squamous"`, `"squamous"`. *(baseline characteristic; modestly prognostic)*

`ecog` ECOG performance status at baseline, integer (0 or 1). *(baseline characteristic; strongly prognostic for PFS and OS)*

`prior_tx` Number of prior lines of systemic therapy, integer (1 or 2). *(baseline characteristic; prognostic — patients with 2 prior lines tend to do worse)*

`smoking` Smoking history, character: `"never"`, `"previous"`, `"current"`. *(baseline characteristic; modestly prognostic and also a correlate of IO benefit through bTMB)*

`sld` Baseline sum of longest diameters of target lesions per RECIST 1.1, mm (numeric). *(baseline characteristic; strongly prognostic — tumor burden)*

`metsites` Number of metastatic sites at enrollment, integer. *(baseline characteristic; strongly prognostic — disease burden)*

`kras` *KRAS* mutation status from CRF, character: `"negative"`, `"positive"`; `NA` when not tested. *(baseline characteristic; weakly / inconsistently prognostic; possible predictive signal for IO)*

`egfr` *EGFR* mutation status from CRF, character: `"negative"`, `"positive"`; `NA` when not tested. A single T790M patient is coded `"positive"`. *(baseline characteristic; weakly prognostic in IO-treated populations; strongly predictive of differential treatment effect — EGFR-positive patients typically derive less benefit from anti-PD-L1)*

`eml4` *EML4-ALK* rearrangement status from CRF, character: `"negative"`, `"positive"`; `NA` when not tested. *(baseline characteristic; analogous to* `egfr` *in interpretation — predictive of reduced IO benefit)*

Details

POPLAR's trial-level eligibility criteria (locally advanced or metastatic NSCLC after platinum failure, ECOG 0–1, measurable disease, no prior anti-PD-L1/PD-1 therapy, adequate organ function, etc.) were applied **before** randomization, so the n = 287 ITT cohort is randomized 1:1. The bTMB assay was performed retrospectively on banked baseline plasma; all assay-derived variables therefore reflect quantities present before treatment exposure, but were generated post-randomization in calendar time. *EGFR* and *EML4-ALK* mutation status are CRF variables collected at screening and can be used to subset without compromising randomization. Variant-level information (permutation chromosome, position, gene, protein change, etc.) was released alongside this table but is not included here; consult the source supplementary file if needed.

Variable role labels

Each variable in the format section above carries a role tag in italic parentheses at the end of its description. The tags combine two dimensions:

- **Baseline characteristic** — measured (or, for the bTMB assay, derived from material collected) at the baseline visit before the first dose of study treatment. Using such variables as covariates does not break randomization in expectation, because they are functions of pre-treatment quantities only.
- **Prognostic** — based on the clinical-oncology literature for previously treated advanced NSCLC, whether the variable has been reported to be associated with PFS or OS independent of treatment assignment. "Predictive" indicates association with differential atezolizumab vs docetaxel benefit rather than with outcome per se. Strength qualifiers (strong / modest / weak) are the author's reading of the literature and are no substitute for a formal analysis on the dataset at hand.

Variables that are outcomes, identifiers, or treatment assignment carry a single role tag in place of the two-dimensional tag.

Pre- vs post-randomization variables

For users planning to apply PATED or any analysis that relies on baseline covariates being balanced across arms:

Pre-randomization (collected at screening; safe to condition on): `age`, `sex`, `race`, `histology`, `ecog`, `prior_tx`, `smoking`, `sld`, `metsites`, `kras`, `egfr`, `eml4`.

Pre-treatment but derived post-randomization (measured on the baseline blood draw, before first dose; empirically b `btmb`, `msaf`, `cfdna_ng`, `coverage`, `qc`, `bep`.

Post-randomization outcomes (must not be used as covariates): `pfs`, `pfs_event`, `os`, `os_event`, `bcor`.

Conditioning on the biomarker-evaluable population (`bep == TRUE`) or further restricting to `!(egfr %in% "positive") & !(eml4 %in% "positive")` is a selection on pre-treatment variables and does not break randomization in expectation; Supp. Tables 3 and 5 of the source paper confirm empirical arm-balance. Users should still verify arm-balance on their working subset (e.g. with **tableone**) before invoking methods that assume it.

Source

Built from Supplementary Table 8 (Excel file MOESM3) of: Gandara DR, Paul SM, Kowanetz M, Schleifman E, Zou W, Li Y, Rittmeyer A, Fehrenbacher L, Otto G, Malboeuf C, Lieber DS, Lipson D, Silterra J, Amler L, Riehl T, Cummings CA, Hegde PS, Sandler A, Ballinger M, Fabrizio D, Mok T, Shames DS. Blood-based tumor mutational burden as a predictor of clinical benefit in non-small-cell lung cancer patients treated with atezolizumab. *Nature Medicine* 2018; 24(9):1441–1448. doi:10.1038/s41591018013 43. Supplementary file downloaded from https://www.nature.com/articles/s41591-018-0134-3. See `data-raw/poplar_oak.R` in the package source for the exact cleaning steps. Redistribution in this package is for non-commercial research and teaching use; users intending other use should verify the licensing terms of the Springer Nature supplementary materials. **Always cite the original publication when using this dataset.**

References

Fehrenbacher L, Spira A, Ballinger M, Kowanetz M, Vansteenkiste J, Mazieres J, Park K, Smith D, Artal-Cortes A, Lewanski C, Braiteh F, Waterkamp D, He P, Zou W, Chen DS, Yi J, Sandler A, Rittmeyer A; POPLAR Study Group. Atezolizumab versus docetaxel for patients with previously treated non-small-cell lung cancer (POPLAR): a multicentre, open-label, Phase 2 randomised controlled trial. *Lancet* 2016; 387(10030):1837–1846. doi:10.1016/S01406736(16)005870.

Examples

```
data(poplar)
table(poplar$arm, useNA = "ifany")
summary(poplar$btmb)
# Biomarker-evaluable subset used in the published bTMB analyses
poplar_bep <- subset(poplar, bep)
```

print.summary.jointCovariance *Title Summarize an Analysis of Multiple Outcomes.*

Description

Summarize an analysis of multiple outcomes.

Usage

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

Arguments

x	an object returned by `jointCovariance()`.
...	for debugging only.

Value

an invisible object.

Examples

```
## no example
```

quantile_ *Creating Objects of Group Quantile Differences*

Description

`quantile_` is a wrapper function creating an object that, for each requested probability, computes the difference between the two arms' sample quantiles of the outcome. The object is passed to `jointCovariance` or `pated` through `...`. Because the empirical-quantile estimator has no tractable closed-form score, this engine is available only through the bootstrap path (`nboot > 0`).

Usage

```
quantile_(formula, probs = c(0.25, 0.5, 0.75), data_index = 1)
```

Arguments

formula	a two-sided formula y ~ arm where the right-hand side is a binary grouping variable.
probs	numeric vector of probabilities in (0, 1). By default the first quartile, median, and third quartile.
data_index	integer. Index of the data frame in the data argument of jointCovariance to be used.

---

simulateMoData *Generating Data for Simulation and Testing*

Description

simulateMoData generates data for simulation and testing purposes.

Usage

```
simulateMoData(n = 500, hr = 0.8, seed = NULL)
```

Arguments

n	an integer for total sample size of a randomized control trial of two arms.
hr	hazard ratio of treatment.
seed	random seed. By default NULL for no seed being specified.

---

summary.jointCovariance *Object Summaries*

Description

summary method for class jointCovariance.

Usage

```
## S3 method for class 'jointCovariance'
summary(object, model_index = NULL, ...)
```

Arguments

object	an object returned by jointCovariance().
model_index	NULL if displaying summary of all fitted models; otherwise, an integer indicating the fitted model.
...	for debugging only

Value

a list

`vcov.jointCovariance` *Calculate Variance-Covariance Matrix for a Fitted Model Object*

Description

Returns the variance-covariance matrix of the main parameters of fitted model objects. The "main" parameters of models correspond to those returned by `coef`.

Usage

```
## S3 method for class 'jointCovariance'
vcov(object, model_index = NULL, ...)
```

Arguments

`object`	an object returned by `jointCovariance()`.
`model_index`	`NULL` if displaying covariance matrix of all fitted models; otherwise, an integer indicating the fitted model.
`...`	for debugging only

Value

a matrix of covariance of all estimates

`winratio_` *Creating Objects of Hierarchical Log Win-Ratio Statistic*

Description

`winratio_` creates an object to be passed into `jointCovariance` or `pated` through its `...` argument. The object defines a hierarchical win-ratio statistic across a list of endpoints, each declared by `nb_tte()`, `nb_continuous()`, or `nb_binary()`.

Usage

```
winratio_(formula, endpoints, data_index = 1)
```

Arguments

formula	a two-sided R formula <label> ~ arm. The LHS is used purely as a row label in pated() output; the RHS must contain exactly one variable, the column in data holding treatment-arm assignment.
endpoints	a non-empty list of endpoint specs built by nb_tte(), nb_continuous(), or nb_binary(). The order of the list encodes the hierarchical priority: endpoint 1 is checked first; if it ties, the pair falls through to endpoint 2; and so on.
data_index	integer. Index of the data frame in the data argument of jointCovariance to be used.

Details

The fitted coefficient is on the log scale:

$$\widehat{\theta} = \log(\widehat{WR}) = \log(\widehat{\pi}_W / \widehat{\pi}_L)$$

where $\widehat{\pi}_W$ and $\widehat{\pi}_L$ are the proportions of all control-treatment pairs where the treatment subject wins or loses, respectively. Tied pairs remain in the denominator of both proportions but do not contribute to either numerator.

The raw win ratio can be recovered by exponentiating the coefficient. The log scale is used because it gives the standard large-sample Wald representation and maps the null win ratio of 1 to 0.

The arm reference level is inferred from the arm column the same way model.matrix(~ arm) would: levels(arm)[1] for factor, the smaller value for numeric or logical, and the alphabetically first value for character. To override, convert the column to a factor with the desired level order before calling winratio_().

Value

An object of class c("jc_spec_winratio", "jc_spec").

See Also

nb_tte(), nb_continuous(), nb_binary(), jointCovariance(), pated().

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