Package: beastt (via r-universe)

September 7, 2024

Title Bayesian Evaluation, Analysis, and Simulation Software Tools for Trials

Version 0.0.2

Description Bayesian dynamic borrowing with covariate adjustment via inverse probability weighting for simulations and data analyses in clinical trials. This makes it easy to use propensity score methods to balance covariate distributions between external and internal data.

License Apache License (>= 2)

URL https://gsk-biostatistics.github.io/beastt/,

https://github.com/GSK-Biostatistics/beastt

BugReports https://github.com/GSK-Biostatistics/beastt/issues

Suggests knitr, rmarkdown, spelling, testthat (>= 3.0.0), tibble

Config/testthat/edition 3

Encoding UTF-8

Roxygen list(markdown = TRUE)

RoxygenNote 7.3.1

Imports cli, cobalt, dplyr, generics, ggplot2, purrr, rlang, stringr, distributional, tidyr, ggdist, mixtools

VignetteBuilder knitr

Depends R (>= 2.10)

LazyData true

Language en-US

Repository https://gsk-biostatistics.r-universe.dev

RemoteUrl https://github.com/gsk-biostatistics/beastt

RemoteRef HEAD

RemoteSha de59b607d3e76248ae4ffed6bf6172683262ef8f

Contents

calc_post_beta	2
calc_post_norm	3
calc_power_prior_beta	4
calc power prior norm	6
calc prop scr	7
ex hinary df	9
ex_orm df	9
int binary df	10
	10
int_norm_df	11
is_prop_scr	11
plot_dist	12
prop scr dens	13
prop scr hist	14
prop scr love	15
	1.7
robustify_norm	15
	17
	1/

Index

calc_post_beta Calculate Posterior Beta

Description

Calculate a posterior distribution that is beta (or a mixture of beta components). Only the relevant treatment arms from the internal dataset should be read in (e.g., only the control arm if constructing a posterior distribution for the control response rate).

Usage

calc_post_beta(internal_data, response, prior)

Arguments

internal_data	This can either be a propensity score object or a tibble of the internal data.
response	Name of response variable
prior	A distributional object corresponding to a beta distribution or a mixture distri-
	bution of beta components

Details

For a given arm of an internal trial (e.g., the control arm or an active treatment arm) of size N_I , suppose the response data are binary such that $y_i \sim \text{Bernoulli}(\theta)$, $i = 1, \ldots, N_I$. The posterior distribution for θ is written as

$$\pi(\theta \mid \boldsymbol{y}) \propto \mathcal{L}(\theta \mid \boldsymbol{y}) \ \pi(\theta),$$

calc_post_norm

where $\mathcal{L}(\theta \mid \boldsymbol{y})$ is the likelihood of the response data from the internal arm and $\pi(\theta)$ is a prior distribution on θ (either a beta distribution or a mixture distribution with an arbitrary number of beta components). The posterior distribution for θ is either a beta distribution or a mixture of beta components depending on whether the prior is a single beta distribution or a mixture distribution.

Value

distributional object

Examples

calc_post_norm

Calculate Posterior Normal

Description

Calculate a posterior distribution that is normal (or a mixture of normal components). Only the relevant treatment arms from the internal dataset should be read in (e.g., only the control arm if constructing a posterior distribution for the control mean).

Usage

```
calc_post_norm(internal_data, response, prior, internal_sd = NULL)
```

Arguments

internal_data	This can either be a propensity score object or a tibble of the internal data.
response	Name of response variable
prior	A distributional object corresponding to a normal distribution, a t distribution, or a mixture distribution of normal and/or t components
internal_sd	Standard deviation of internal response data if assumed known. It can be left as NULL if assumed unknown

Details

For a given arm of an internal trial (e.g., the control arm or an active treatment arm) of size N_I , suppose the response data are normally distributed such that $y_i \sim N(\theta, \sigma_I^2)$, $i = 1, ..., N_I$. If σ_I^2 is assumed known, the posterior distribution for θ is written as

$$\pi(\theta \mid \boldsymbol{y}, \sigma_I^2) \propto \mathcal{L}(\theta \mid \boldsymbol{y}, \sigma_I^2) \ \pi(\theta),$$

where $\mathcal{L}(\theta \mid \boldsymbol{y}, \sigma_I^2)$ is the likelihood of the response data from the internal arm and $\pi(\theta)$ is a prior distribution on θ (either a normal distribution, a *t* distribution, or a mixture distribution with an arbitrary number of normal and/or *t* components). Any *t* components of the prior for θ are approximated with a mixture of two normal distributions.

If σ_I^2 is unknown, the marginal posterior distribution for θ is instead written as

$$\pi(\theta \mid \boldsymbol{y}) \propto \left\{ \int_0^\infty \mathcal{L}(\theta, \sigma_I^2 \mid \boldsymbol{y}) \ \pi(\sigma_I^2) \ d\sigma_I^2 \right\} \times \pi(\theta).$$

In this case, the prior for σ_I^2 is chosen to be $\pi(\sigma_I^2) = (\sigma_I^2)^{-1}$ such that $\{\int_0^\infty \mathcal{L}(\theta, \sigma_I^2 \mid \boldsymbol{y}) \; \pi(\sigma_I^2) \; d\sigma_I^2\}$ becomes a non-standardized *t* distribution. This integrated likelihood is then approximated with a mixture of two normal distributions.

If internal_sd is supplied a positive value and prior corresponds to a single normal distribution, then the posterior distribution for θ is a normal distribution. If internal_sd = NULL or if other types of prior distributions are specified (e.g., mixture or t distribution), then the posterior distribution is a mixture of normal distributions.

Value

distributional object

Examples

calc_power_prior_beta Calculate Power Prior Beta

Description

Calculate a (potentially inverse probability weighted) beta power prior for the control response rate using external control data.

Usage

```
calc_power_prior_beta(external_data, response, prior)
```

Arguments

external_data	This can either be a prop_scr_obj created by calling create_prop_scr() or a tibble of the external data. If it is just a tibble the weights will be assumed to be 1.
response	Name of response variable
prior	A beta distributional object that is the initial prior for the control response rate before the external control data are observed

Details

Weighted participant-level response data from an external study are incorporated into an inverse probability weighted (IPW) power prior for the control response rate θ_C . When borrowing information from an external control arm of size N_{EC} , the components of the IPW power prior for θ_C are defined as follows:

Initial prior: $\theta_C \sim \text{Beta}(\nu_0, \phi_0)$

IPW likelihood of the external response data y_E with weights \hat{a}_0 : $\mathcal{L}_E(\theta_C \mid y_E, \hat{a}_0) \propto \exp\left(\sum_{i=1}^{N_{EC}} \hat{a}_{0i} \left[y_i \log(\theta_C) + (\sum_{i=1}^{N_{EC}} \hat{a}_{0i} (y_i \log(\theta_C) + (\sum$

IPW power prior:
$$heta_C \mid oldsymbol{y}_E, \hat{oldsymbol{a}}_0 \sim ext{Beta}\left(\sum_{i=1}^{N_{EC}} \hat{a}_{0i}y_i +
u_0, \sum_{i=1}^{N_{EC}} \hat{a}_{0i}(1-y_i) + \phi_0\right)$$

Defining the weights \hat{a}_0 to equal 1 results in a conventional beta power prior.

Value

Beta power prior object

See Also

Other power prior: calc_power_prior_norm()

```
library(distributional)
library(dplyr)
# This function can be used directly on the data
calc_power_prior_beta(external_data = ex_binary_df,
    response = y,
    prior = dist_beta(0.5, 0.5))
# Or this function can be used with a propensity score object
ps_obj <- calc_prop_scr(internal_df = filter(int_binary_df, trt == 0),
    external_df = ex_binary_df,
    id_col = subjid,
    model = ~ cov1 + cov2 + cov3 + cov4)
calc_power_prior_beta(ps_obj,
    response = y,
    prior = dist_beta(0.5, 0.5))</pre>
```

calc_power_prior_norm Calculate Power Prior Normal

Description

Calculate a (potentially inverse probability weighted) normal power prior using external data.

Usage

```
calc_power_prior_norm(
    external_data,
    response,
    prior = NULL,
    external_sd = NULL
)
```

Arguments

external_data	This can either be a prop_scr_obj created by calling create_prop_scr() or a tibble of the external data. If it is just a tibble the weights will be assumed to be 1. Only the external data for the arm(s) of interest should be included in this object (e.g., external control data if creating a power prior for the control mean)
response	Name of response variable
prior	Either NULL or a normal distributional object that is the initial prior for the parameter of interest (e.g., control mean) before the external data are observed
external_sd	Standard deviation of external response data if assumed known. It can be left as NULL if assumed unknown

Details

Weighted participant-level response data from an external study are incorporated into an inverse probability weighted (IPW) power prior for the parameter of interest θ (e.g., the control mean if borrowing from an external control arm). When borrowing information from an external dataset of size N_E , the IPW likelihood of the external response data y_E with weights \hat{a}_0 is defined as

$$\mathcal{L}_E(\theta \mid \boldsymbol{y}_E, \hat{\boldsymbol{a}}_0, \sigma_E^2) \propto \exp\left(-\frac{1}{2\sigma_E^2} \sum_{i=1}^{N_E} \hat{a}_{0i} (y_i - \theta)^2\right).$$

The prior argument should be either a distributional object with a family type of normal or NULL, corresponding to the use of a normal initial prior or an improper uniform initial prior (i.e., $\pi(\theta) \propto 1$), respectively.

The external_sd argument can be a positive value if the external standard deviation is assumed known or left as NULL otherwise. If external_sd = NULL, then prior must be NULL to indicate the use of an improper uniform initial prior for θ , and an improper prior is defined for the unknown external standard deviation such that $\pi(\sigma_E^2) \propto (\sigma_E^2)^{-1}$. The details of the IPW power prior for each case are as follows:

- external_sd = positive value (σ_E^2 known): With either a proper normal or an improper uniform initial prior, the IPW weighted power prior for θ is a normal distribution.
- external_sd = NULL (σ_E^2 unknown): With improper priors for both θ and σ_E^2 , the marginal IPW weighted power prior for θ after integrating over σ_E^2 is a non-standardized t distribution.

Defining the weights \hat{a}_0 to equal 1 results in a conventional normal (or t) power prior if the external standard deviation is known (unknown).

Value

Normal power prior object

See Also

Other power prior: calc_power_prior_beta()

Examples

```
library(distributional)
library(dplyr)
# This function can be used directly on the data
calc_power_prior_norm(ex_norm_df,
  response = y,
  prior = dist_normal(50, 10),
  external_sd = 0.15)
# Or this function can be used with a propensity score object
ps_obj <- calc_prop_scr(internal_df = filter(int_norm_df, trt == 0),</pre>
                        external_df = ex_norm_df,
                        id_col = subjid,
                        model = \sim cov1 + cov2 + cov3 + cov4)
calc_power_prior_norm(ps_obj,
                      response = y,
                      prior = dist_normal(50, 10),
                      external_sd = 0.15)
```

calc_prop_scr Create a Propensity Score Object

Description

Calculate the propensity scores and ATT inverse probability weights for participants from internal and external datasets. Only the relevant treatment arms from each dataset should be read in (e.g., only the control arm from each dataset if creating a hybrid control arm).

Usage

```
calc_prop_scr(internal_df, external_df, id_col, model, ...)
```

Arguments

external_dfExternal dataset with one row per subject and all the variables needed to run the modelid_colName of the column in both datasets used to identify each subject. It must be the same across datasetsmodelModel used to calculate propensity scoresOptional arguments	internal_df	Internal dataset with one row per subject and all the variables needed to run the model
id_colName of the column in both datasets used to identify each subject. It must be the same across datasetsmodelModel used to calculate propensity scoresOptional arguments	external_df	External dataset with one row per subject and all the variables needed to run the model
model Model used to calculate propensity scores Optional arguments	id_col	Name of the column in both datasets used to identify each subject. It must be the same across datasets
Optional arguments	model	Model used to calculate propensity scores
		Optional arguments

Details

For the subset of participants in both the external and internal studies for which we want to balance the covariate distributions (e.g., external control and internal control participants if constructing a hybrid control arm), we define a study-inclusion propensity score for each participant as

$$e(x_i) = P(S_i = 1 \mid x_i),$$

where x_i denotes a vector of baseline covariates for the *i*th participant and S_i denotes the indicator that the participant is enrolled in the internal trial ($S_i = 1$ if internal, $S_i = 0$ if external). The estimated propensity score $\hat{e}(x_i)$ is obtained using logistic regression.

An ATT inverse probability weight is calculated for each individual as

$$\hat{a}_{0i} = \frac{\hat{e}(x_i)}{\hat{P}(S_i = s_i | x_i)} = s_i + (1 - s_i) \frac{\hat{e}(x_i)}{1 - \hat{e}(x_i)}.$$

In a weighted estimator, data from participants in the external study are given a weight of $\hat{e}(x_i)/(1-\hat{e}(x_i))$ whereas data from participants in the internal trial are given a weight of 1.

Value

prop_scr_obj object, with the internal and the external data and the propensity score and inverse probability weight calculated for each subject.

ex_binary_df

Description

This is a simulated dataset used to illustrate Bayesian dynamic borrowing in the case when borrowing from an external control arm with a binary endpoint, where the baseline covariate distributions of the internal and external data are balanced via inverse probability weighting.

Usage

ex_binary_df

Format

ex_binary_df:
A data frame with 150 rows and 6 columns:
subjid Unique subject ID
cov1 Covariate 1, which is normally distributed around 65 with a SD of 10
cov2 Covariate 2, which is binary (0 vs. 1) with about 30% of participants having level 1
cov3 Covariate 3, which is binary (0 vs. 1) with about 40% of participants having level 1
cov4 Covariate 4, which is binary (0 vs. 1) with about 50% of participants having level 1
y Response, which is binary (0 vs. 1)

ex_norm_df

Description

This is a simulated dataset used to illustrate Bayesian dynamic borrowing in the case when borrowing from an external control arm with a normal endpoint, where the baseline covariate distributions of the internal and external data are balanced via inverse probability weighting.

Usage

ex_norm_df

External Normal Control Data for Propensity Score Balancing

Format

ex_norm_df:

A data frame with 150 rows and 6 columns:

subjid Unique subject ID

cov1 Covariate 1, which is normally distributed around 50 with a SD of 10

cov2 Covariate 2, which is binary (0 vs. 1) with about 20% of participants having level 1

cov3 Covariate 3, which is binary (0 vs. 1) with about 60% of participants having level 1

cov4 Covariate 4, which is binary (0 vs. 1) with about 30% of participants having level 1

y Response, which is normally distributed with a SD of 0.15

int_binary_df

Internal Binary Data for Propensity Score Balancing

Description

This is a simulated dataset used to illustrate Bayesian dynamic borrowing in the case when borrowing from an external control arm with a binary endpoint, where the baseline covariate distributions of the internal and external data are balanced via inverse probability weighting.

Usage

int_binary_df

Format

int_binary_df:

A data frame with 160 rows and 7 columns:

subjid Unique subject ID

cov1 Covariate 1, which is normally distributed around 62 with an sd of 8

cov2 Covariate 2, which is binary (0 vs. 1) with about 40% of participants having level 1

cov3 Covariate 3, which is binary (0 vs. 1) with about 40% of participants having level 1

cov4 Covariate 4, which is binary (0 vs. 1) with about 60% of participants having level 1

trt Treatment indicator, where 0 = control and 1 = active treatment

y Response, which is binary (0 vs. 1)

10

11

int_norm_df

Description

This is a simulated dataset used to illustrate Bayesian dynamic borrowing in the case when borrowing from an external control arm with a normal endpoint, where the baseline covariate distributions of the internal and external data are balanced via inverse probability weighting.

Usage

int_norm_df

Format

int_norm_df:
A data frame with 120 rows and 7 columns:
subjid Unique subject ID
cov1 Covariate 1, which is normally distributed around 55 with a SD of 8
cov2 Covariate 2, which is binary (0 vs. 1) with about 30% of participants having level 1
cov3 Covariate 3, which is binary (0 vs. 1) with about 50% of participants having level 1
cov4 Covariate 4, which is binary (0 vs. 1) with about 30% of participants having level 1
trt Treatment indicator, where 0 = control and 1 = active treatment
y Response, which is normally distributed with a SD of 0.15

is_prop_scr

Test If Propensity Score Object

Description

Test If Propensity Score Object

Usage

is_prop_scr(x)

Arguments ×

Object to test

Value

Boolean

Examples

plot_dist Plot Distribution

Description

Plot Distribution

Usage

plot_dist(...)

Arguments

... Distributional object(s) to plot. When passing multiple objects naming them will change the labels in the plot, else they will use the distributional format

Value

ggplot object that is the density of the provided distribution

Examples

```
library(distributional)
plot_dist(dist_normal(0, 1))
#Plotting Multiple
plot_dist(dist_normal(0, 1), dist_normal(10, 5))
plot_dist('Prior' = dist_normal(0, 1), 'Posterior' = dist_normal(10, 5))
```

12

prop_scr_dens

Description

Plot overlapping density curves of the propensity scores for both the internal and external participants, or plot external IPWs.

Usage

```
prop_scr_dens(
    x,
    variable = c("propensity score", "ps", "inverse probability weight", "ipw"),
    ...
)
```

Arguments

х	Propensity score object
variable	Variable to plot. It must be either a propensity score ("ps" or "propensity score") or inverse probability weight ("ipw" or "inverse probability weight")
	Optional arguments for geom_density

Value

ggplot object

prop_scr_hist

Description

Plot overlapping histograms of the propensity scores for both the internal and external participants, or plot external IPWs.

Usage

```
prop_scr_hist(
    x,
    variable = c("propensity score", "ps", "inverse probability weight", "ipw"),
    ...
)
```

Arguments

х	Propensity score object
variable	Variable to plot. It must be either a propensity score ("ps" or "propensity score") or inverse probability weight ("ipw" or "inverse probability weight")
	Optional arguments for geom_histogram

Value

ggplot object

prop_scr_love

Description

Plot the unadjusted and IPW-adjusted absolute standardized mean differences for each covariate.

Usage

```
prop_scr_love(x, reference_line = NULL, ...)
```

Arguments

х	Propensity score object
reference_line	Numeric value of where along the x-axis the vertical reference line should be placed
	Optional options for geom_point

Value

ggplot object

Examples

robustify_norm Robustify Normal Distributions

Description

Adds vague normal component, where the level of vagueness is controlled by the n parameter

Usage

```
robustify_norm(prior, n, weights = c(0.5, 0.5))
```

Arguments

prior	Normal distributional object
n	Number of theoretical participants
weights	Vector of weights, where the first number corresponds to the informative com- ponent and the second is the vague

Details

In cases with a normal endpoint, a robust mixture prior can be created by adding a vague normal component to any normal prior with mean θ and variance σ^2 . The vague component is calculated to have the same mean θ and variance equal to $\sigma^2 \times n$, where n is the specified number of theoretical participants. If robustifying a normal power prior that was calculated from external control data and n is defined as the number of external control participants, and the vague component would then correspond to one external control participant's worth of data.

Value

mixture distribution

```
library(distributional)
robustify_norm(dist_normal(0,1), n = 15)
```

Index

* datasets ex_binary_df, 9 ex_norm_df, 9 int_binary_df, 10 int_norm_df, 11 * power prior calc_power_prior_beta, 4 calc_power_prior_norm, 6 calc_post_beta, 2 calc_post_norm, 3 calc_power_prior_beta, 4, 7 calc_power_prior_norm, 5, 6 calc_prop_scr,7 ex_binary_df, 9 ex_norm_df, 9 int_binary_df, 10 int_norm_df, 11 is_prop_scr, 11 $plot_dist, 12$ prop_scr_dens, 13 prop_scr_hist, 14 prop_scr_love, 15 robustify_norm, 15