## Package: beastt (via r-universe)

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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>

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### <span id="page-1-0"></span>Contents



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



#### 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  $y_i \sim \text{Bernoulli}(\theta)$ ,  $i = 1, ..., N_I$ . The posterior distribution for  $\theta$  is written as

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

#### <span id="page-2-0"></span>calc\_post\_norm 3

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

```
library(dplyr)
library(distributional)
calc_post_beta(internal_data = filter(int_binary_df, trt == 1),
                              response = y,
                              prior = dist_beta(0.5, 0.5)
```
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



#### 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  $\sigma_i^2$ is assumed known, the posterior distribution for  $\theta$  is written as

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

<span id="page-3-0"></span>where  $\mathcal{L}(\theta | y, \sigma_i^2)$  is the likelihood of the response data from the internal arm and  $\pi(\theta)$  is a prior distribution on  $\theta$  (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  $\theta$  are approximated with a mixture of two normal distributions.

If  $\sigma_I^2$  is unknown, the marginal posterior distribution for  $\theta$  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  $\sigma_I^2$  is chosen to be  $\pi(\sigma_I^2) = (\sigma_I^2)^{-1}$  such that  $\left\{ \int_0^\infty \mathcal{L}(\theta, \sigma_I^2 \mid \mathbf{y}) \pi(\sigma_I^2) d\sigma_I^2 \right\}$ 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  $\theta$  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

```
library(distributional)
library(dplyr)
post_treated <- calc_post_norm(internal_data = filter(int_norm_df, trt == 1),
                               response = y,prior = dist_normal(50, 10),
                               interval_s d = 0.15
```
<span id="page-3-1"></span>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)
```
#### <span id="page-4-0"></span>**Arguments**



#### 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  $\theta_C$ . When borrowing information from an external control arm of size  $N_{EC}$ , the components of the IPW power prior for  $\theta_C$ are defined as follows:

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

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

**IPW power prior:** 
$$
\theta_C
$$
 |  $\mathbf{y}_E, \hat{\mathbf{a}}_0 \sim \text{Beta}\left(\sum_{i=1}^{N_{EC}} \hat{a}_{0i} y_i + \nu_0, \sum_{i=1}^{N_{EC}} \hat{a}_{0i} (1 - y_i) + \phi_0\right)$ 

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\(](#page-5-1))

```
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 = \sim cov1 + cov2 + cov3 + cov4)
calc_power_prior_beta(ps_obj,
  response = y,
  prior = dist\_beta(0.5, 0.5))
```
<span id="page-5-1"></span><span id="page-5-0"></span>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



#### 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  $\theta$  (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  $\theta$ , 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:

- <span id="page-6-0"></span>external\_sd = positive value ( $\sigma_E^2$  **known):** With either a proper normal or an improper uniform initial prior, the IPW weighted power prior for  $\theta$  is a normal distribution.
- external\_sd = NULL ( $\sigma_E^2$  unknown): With improper priors for both  $\theta$  and  $\sigma_E^2$ , the marginal IPW weighted power prior for  $\theta$  after integrating over  $\sigma_E^2$  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\(](#page-3-1))

#### 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_s d = 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),
                       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



#### 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

$$
e(x_i) = P(S_i = 1 | x_i),
$$

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  $\hat{e}(x_i)/(1-\epsilon)$  $\hat{e}(x_i)$ ) 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.

```
# This can be used for both continuous and binary data
library(dplyr)
# Continuous
calc_prop_scr(internal_df = filter(int_norm_df, trt == 0),
                       external_df = ex_norm_df,
                       id_col = subjid,
                       model = \sim cov1 + cov2 + cov3 + cov4)
# Binary
calc_prop_scr(internal_df = filter(int_binary_df, trt == 0),
                       external_df = ex_binary_df,
                       id_col = subjid,
                       model = \sim cov1 + cov2 + cov3 + cov4)
```
<span id="page-8-0"></span>

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  $(0 \text{ vs. } 1)$ 

#### 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

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  $(0 \text{ vs. } 1)$ 

<span id="page-9-0"></span>

<span id="page-10-0"></span>

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

x Object to test

#### Value

Boolean

#### Examples

```
library(dplyr)
x \leq - \text{calc\_prop\_scr(internal\_df = filter(int\_norm\_df, trt == 0),external_df = ex_norm_df,
                         id_col = subjid,
                         model = \sim cov1 + cov2 + cov3 + cov4)
is_prop_scr(x)
```
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

```
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))
```
<span id="page-11-0"></span>

<span id="page-12-0"></span>

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"),
  ...
\mathcal{L}
```
#### Arguments



#### Value

ggplot object

```
library(dplyr)
ps_obj <- calc_prop_scr(internal_df = filter(int_norm_df, trt == 0),
                       external_df = ex_norm_df,
                       id_{col} = subjid,model = \sim cov1 + cov2 + cov3 + cov4)
# Plotting the Propensity Scores
prop_scr_dens(ps_obj)
# Or plotting the inverse probability weights
prop_scr_dens(ps_obj, variable = "ipw")
```
<span id="page-13-0"></span>

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"),
  ...
\mathcal{L}
```
#### Arguments



#### Value

ggplot object

```
library(dplyr)
ps_obj <- calc_prop_scr(internal_df = filter(int_norm_df, trt == 0),
                       external_df = ex_norm_df,
                       id_col = subjid,
                       model = \sim cov1 + cov2 + cov3 + cov4)
# Plotting the Propensity Scores
prop_scr_hist(ps_obj)
# Or plotting the inverse probability weights
prop_scr_hist(ps_obj, variable = "ipw")
```
<span id="page-14-0"></span>

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

#### Usage

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



#### Value

ggplot object

#### Examples

```
library(dplyr)
ps_obj <- calc_prop_scr(internal_df = filter(int_norm_df, trt == 0),
                      external_df = ex_norm_df,
                       id_col = subjid,
                       model = \sim cov1 + cov2 + cov3 + cov4)# Plotting the Propensity Scores
prop_scr_love(ps_obj, reference_line = 0.1)
```
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



#### 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  $\theta$  and variance  $\sigma^2$ . The vague component is calculated to have the same mean  $\theta$  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)
```
# <span id="page-16-0"></span>Index

∗ datasets ex\_binary\_df, [9](#page-8-0) ex\_norm\_df, [9](#page-8-0) int\_binary\_df, [10](#page-9-0) int\_norm\_df, [11](#page-10-0) ∗ power prior calc\_power\_prior\_beta, [4](#page-3-0) calc\_power\_prior\_norm, [6](#page-5-0) calc\_post\_beta, [2](#page-1-0) calc\_post\_norm, [3](#page-2-0) calc\_power\_prior\_beta, [4,](#page-3-0) *[7](#page-6-0)* calc\_power\_prior\_norm, *[5](#page-4-0)*, [6](#page-5-0) calc\_prop\_scr, [7](#page-6-0) ex\_binary\_df, [9](#page-8-0) ex\_norm\_df, [9](#page-8-0) int\_binary\_df, [10](#page-9-0) int\_norm\_df, [11](#page-10-0) is\_prop\_scr, [11](#page-10-0) plot\_dist, [12](#page-11-0) prop\_scr\_dens, [13](#page-12-0) prop\_scr\_hist, [14](#page-13-0) prop\_scr\_love, [15](#page-14-0) robustify\_norm, [15](#page-14-0)