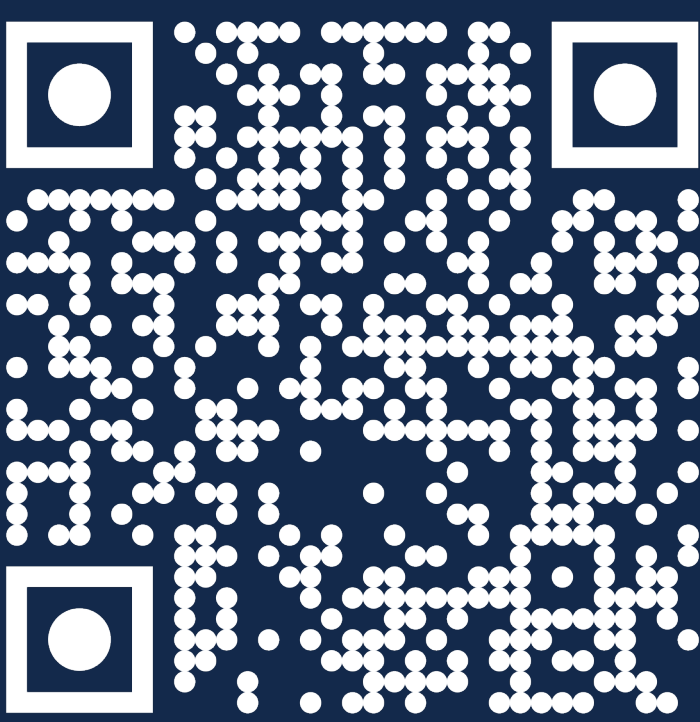
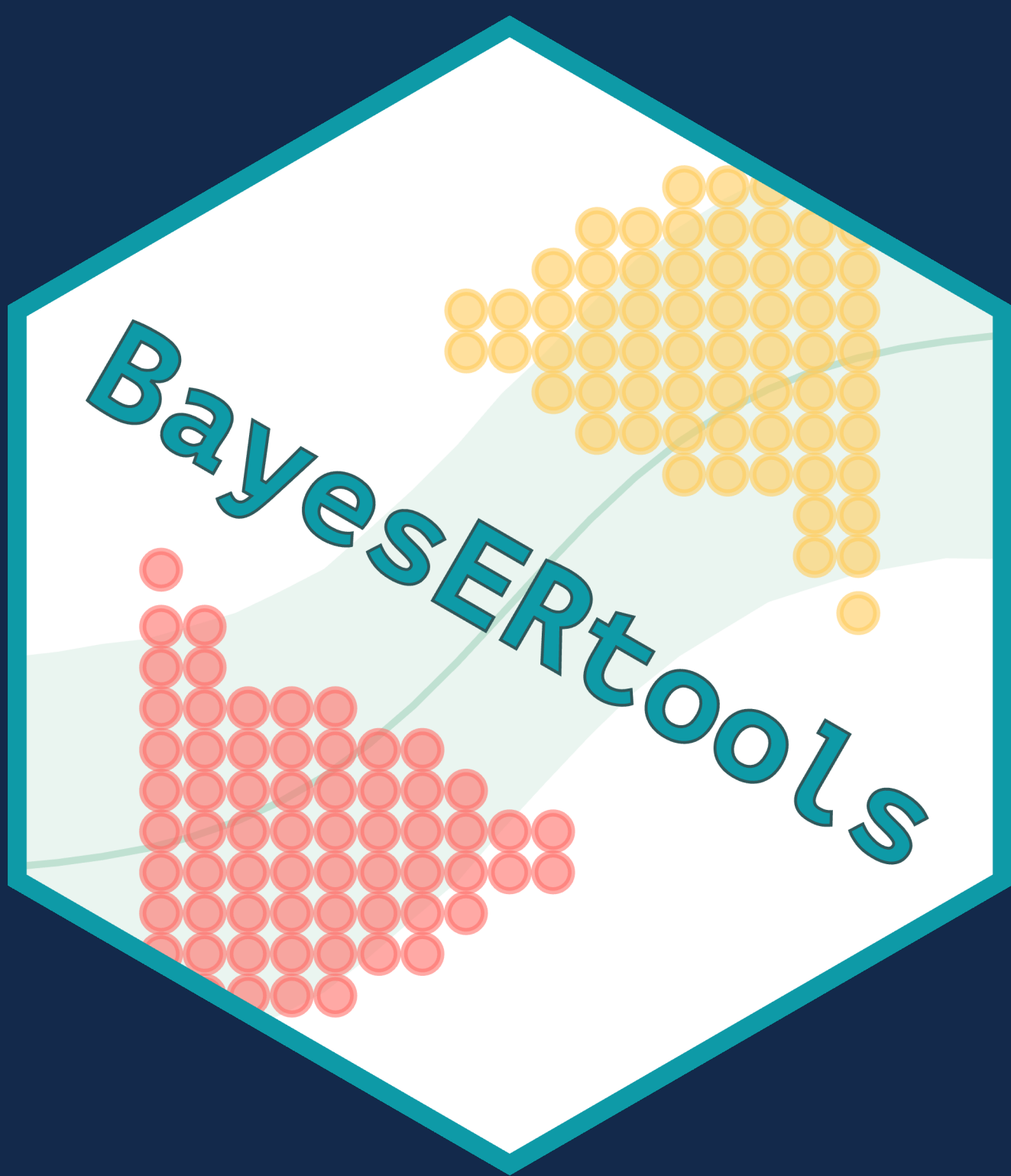


BayesERtools enables streamlined workflows for cross-sectional E-R analysis with Bayesian framework & aid in quantitative clinical drug development decisions



BayesERtools: R package for exposure-response analysis with Bayesian approaches

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<https://genentech.github.io/BayesERtools/>, <https://genentech.github.io/BayesERbook/>

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Background

Exposure-response (ER) analysis is an essential component in clinical pharmacology to assess the relationship between drug exposure and therapeutic or adverse outcomes. Bayesian approaches are particularly suited for ER analysis by enabling natural handling of uncertainty through posterior samples and informative clinical trial simulations, as well as implementing learn-and-confirm cycles. The newly developed R package, BayesERtools, is designed to facilitate the use of Bayesian approaches for ER modeling by providing a streamlined user interface to easily execute common ER modeling tasks.

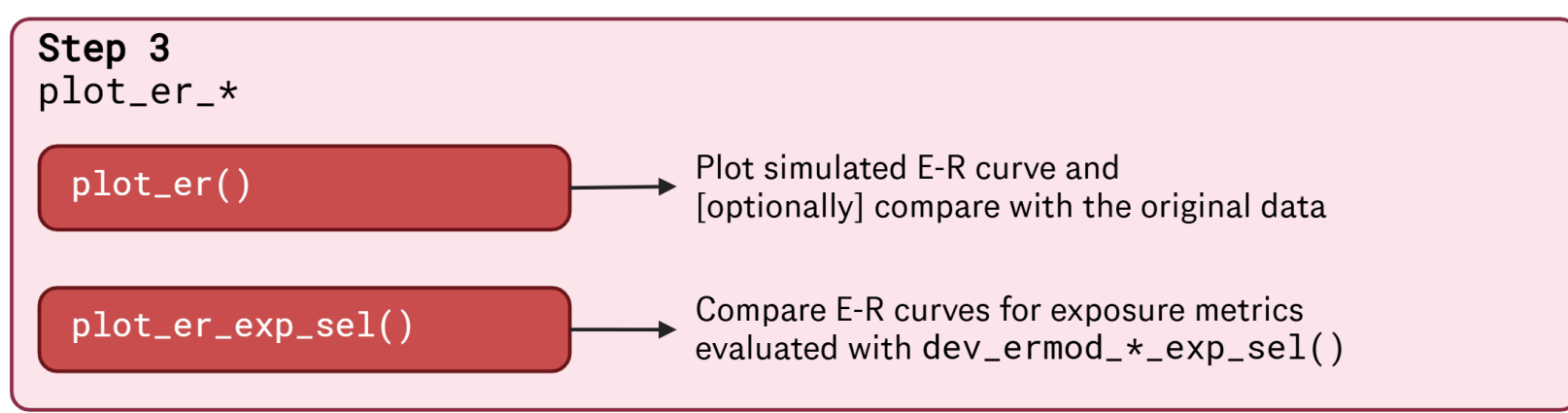
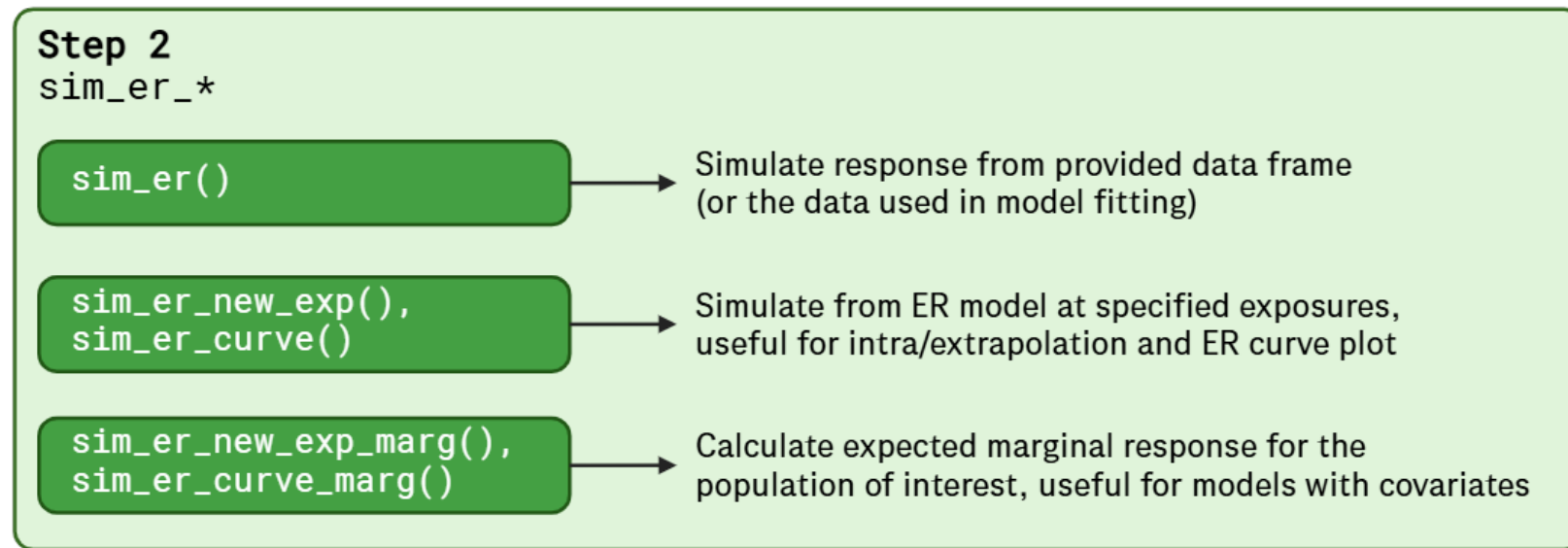
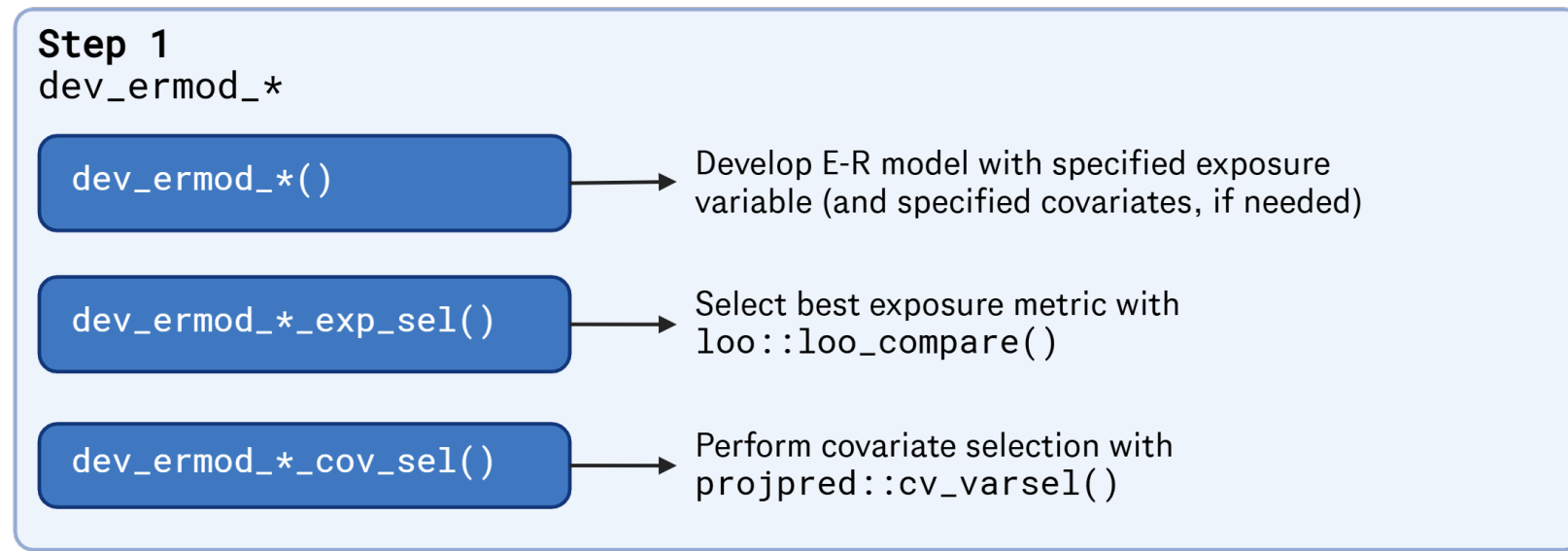
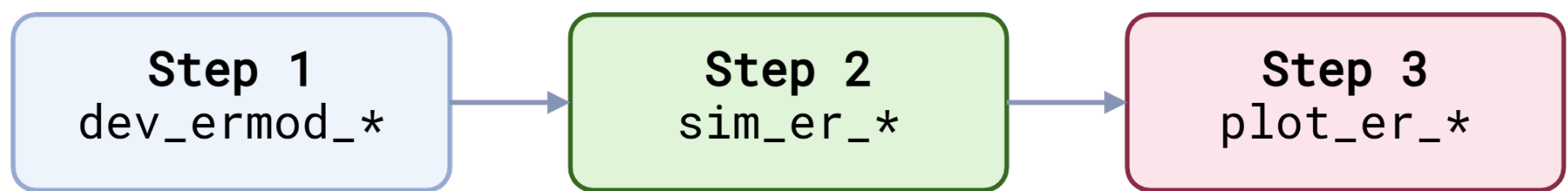
Models & functions

BayesERtools currently supports the development of the following models, which are expected to cover majority of cross-sectional ER analysis:

	Binary endpoint		Continuous endpoint	
	Linear (logit)	E _{max} (logit)	Linear	E _{max}
backend	rstanarm	rstanemax	rstanarm	rstanemax
reference	♂	♂	♂	♂
develop model	✓	✓	✓	✓
simulate & plot ER	✓	✓	✓	✓
exposure metrics selection	✓	✓	✓	✓
covariate selection	✓	✗	✓	✗
covariate forest plot	✓	✗	●	✗

✓ Available, ● In plan/under development, ✗ Not in a current plan

Analysis can be performed in the following steps: model development, simulation, and visualization.



Below are the critical dependencies (non-exhaustive):

- Stan/rstan (core tool for Bayesian inference)
- rstanarm (linear and logistic regression models)
- rstanemax (Emax models)
- posterior/tidybayes (post-processing)
- loo (model comparison/evaluation)
- projpred (covariate selection)

Example workflow & outputs for binary E-R model

1. Setup and load data

```
library(tidyverse)
library(BayesERtools)
library(posterior)
library(here)
library(gt)
```

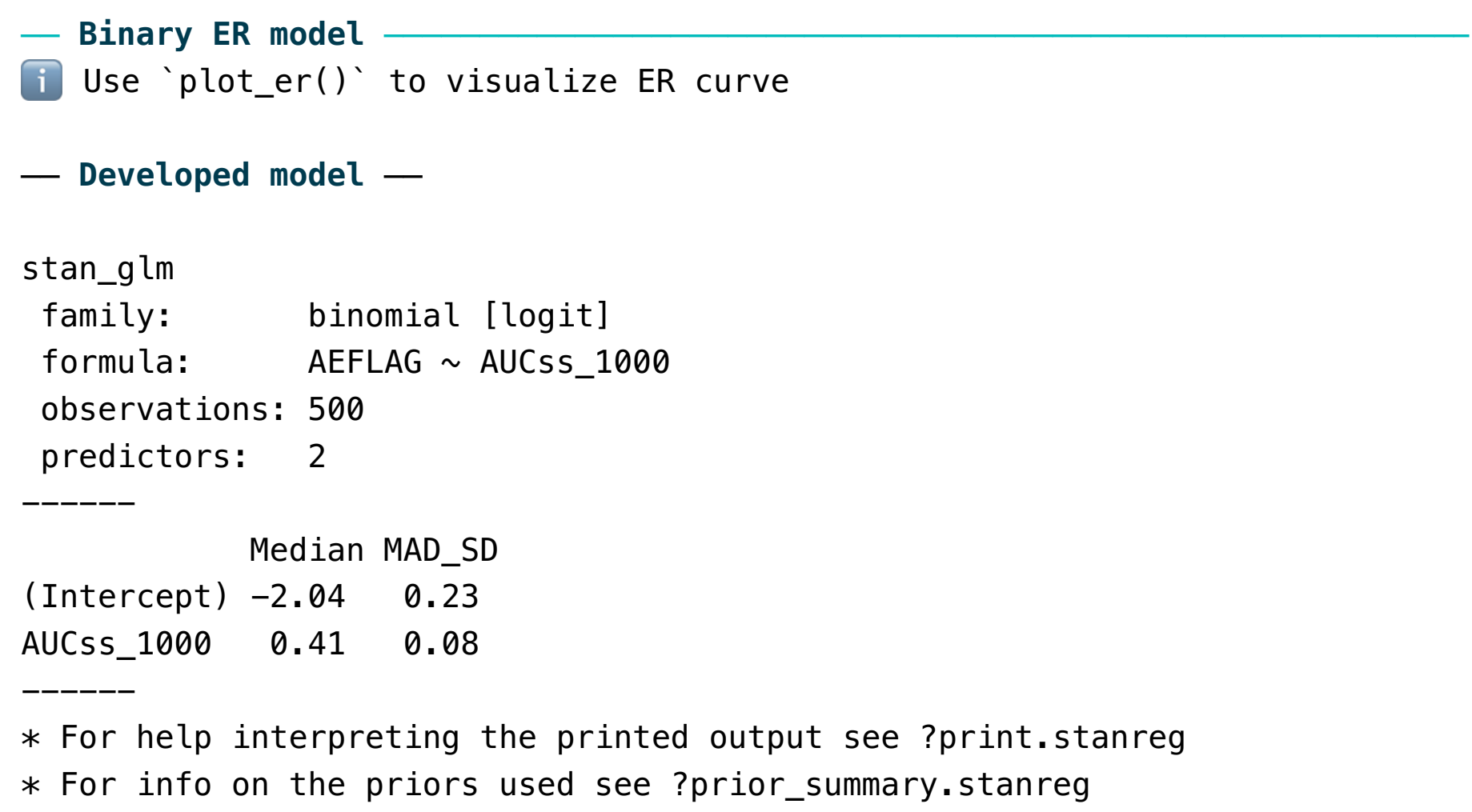
We use an example simulated dataset included in BayesERtools package.

```
data(d_sim_binom_cov)
df_er_ae_hgly2 <-
  d_sim_binom_cov |>
  # Grade>2 hyperglycemia
  filter(AETYPE == "hgly2")
```

2. Basic model development

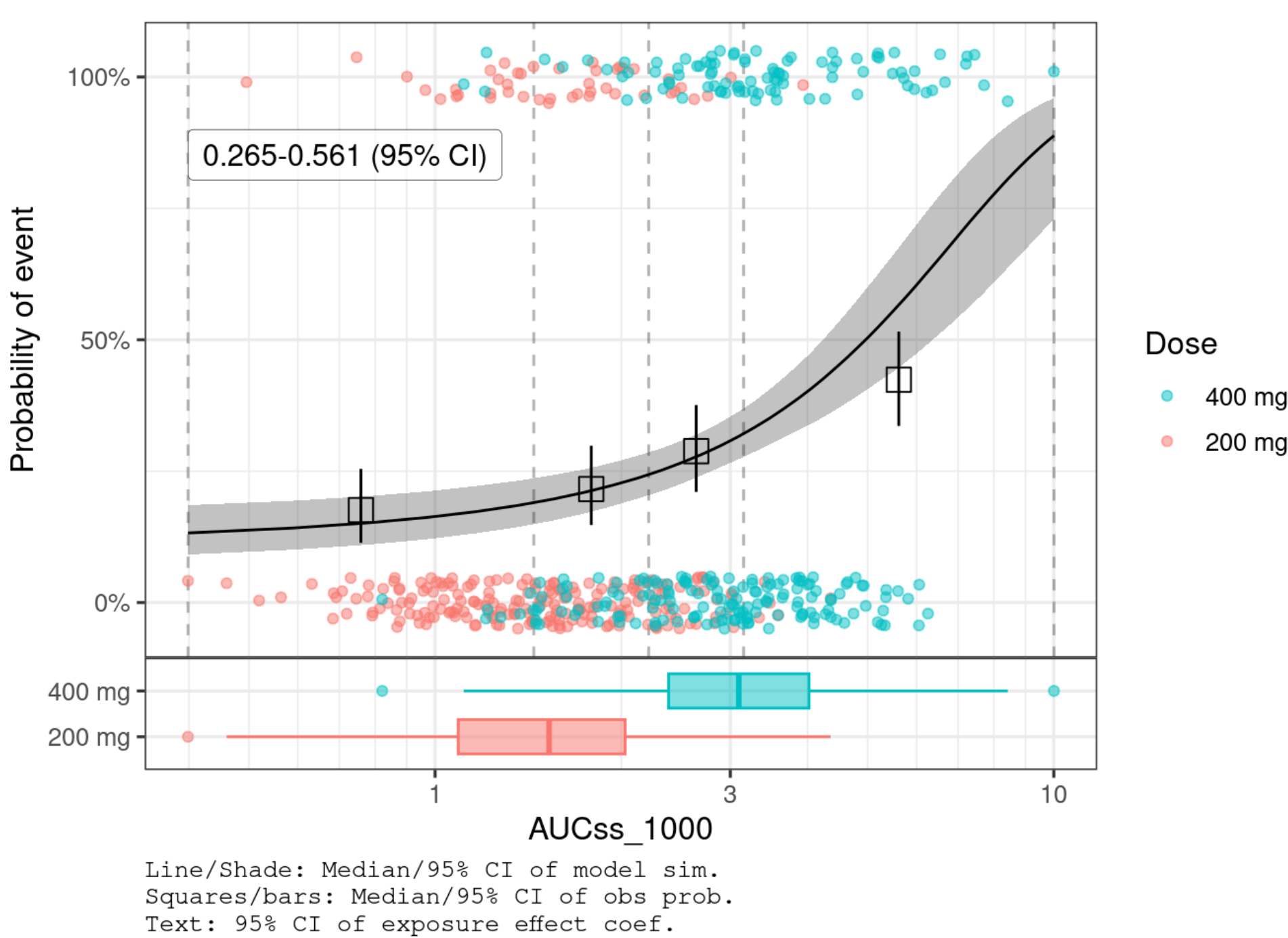
Use `dev_ermod_bin()` function to develop a model.

```
set.seed(1234)
ermod_bin <- dev_ermod_bin(
  data = df_er_ae_hgly2,
  var_resp = "AEFLAG",
  var_exposure = "AUCss_1000" # AUCss/1000
)
```



We can compare the observed data with the model fit using `plot_er_gof()` function.

```
plot_er_gof(ermod_bin, var_group = "Dose",
  show_coef_exp = TRUE) *
  xgxr::xgx_scale_x_log10()
```



3. Covariate model development

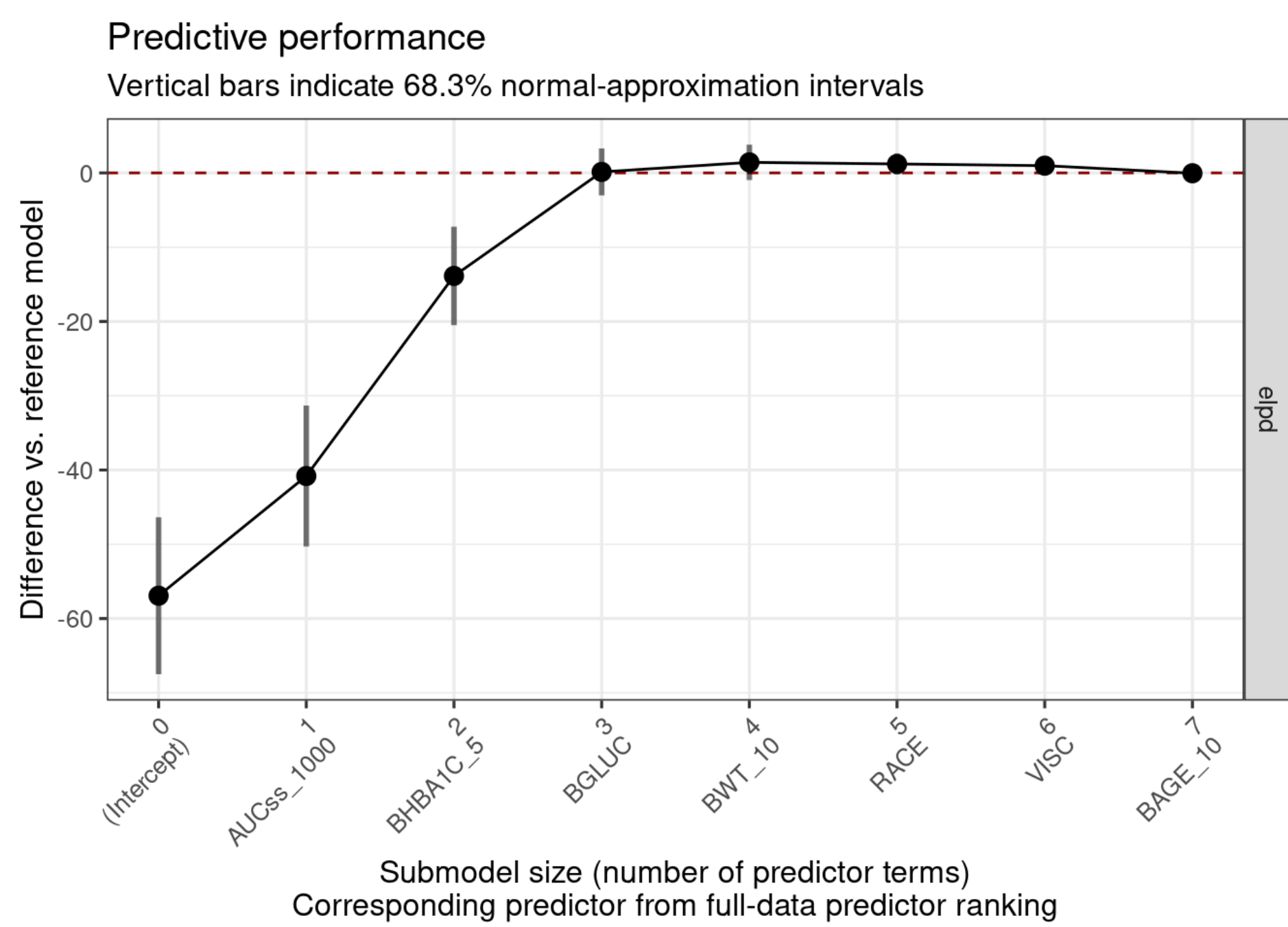
`dev_ermod_bin_cov_sel()` function can be used to select the covariates (using *projpred* under the hood: <https://mc-stan.org/projpred/>)

```
set.seed(1234)
var_cov_ae_hgly2 <- c("BAGE_10", "BWT_10",
  "RACE", "VISC", "BHBA1C_5", "BGLUC") # List of
covariates
```

```
ermod_bin_cov_sel <- dev_ermod_bin_cov_sel(
  data = df_er_ae_hgly2,
  var_resp = "AEFLAG",
  var_exposure = "AUCss_1000",
  var_cov_candidate = var_cov_ae_hgly2,
  verbosity_level = 2
)
```

HbA1c (BHBA1C_5) and glucose (BGLUC) added to “projection” to the reference (full) model, in addition to the exposure metric AUCss_1000.

`plot_submod_performance(ermod_bin_cov_sel)`



You can visualize the effect of the covariates with `plot_coveff()`.

```
coveffsim <- sim_coveff(ermod_bin_cov_sel)
plot_coveff(coveffsim)
```

