

Shiny MAP Prior Manual

Maintainer: Alexander Stemke

November 2020

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1 Introduction

This manual shall give guidance in the use and function of the MAP Prior Shiny App. The app allows you to retrieve a Meta Analytic Predictive Prior by using Bayesian Hierarchical models. It is also possible to create prior distributions without historical information.

The app uses the R-Package RBesT (R Bayesian Evidence Synthesis Tools) for calculations. For further information of the mathematical background we recommend to have a look in the Vignettes and RBesT itself.

This app is not validated and still in development.

Authors: Dr. Martin Oliver Sailer, Alexander Stemke

Contributors: Steven Brooks, Sahin Saide

For any questions, remarks, errors or feedback please contact:

Maintainer:
alexander.stemke@boehringer-ingelheim.com

The manual will introduce every tab on its own.

2 Main Page

This is the default main page, which will be displayed when you start the app. It is strongly recommended to use the app in fullscreen for better user experience.

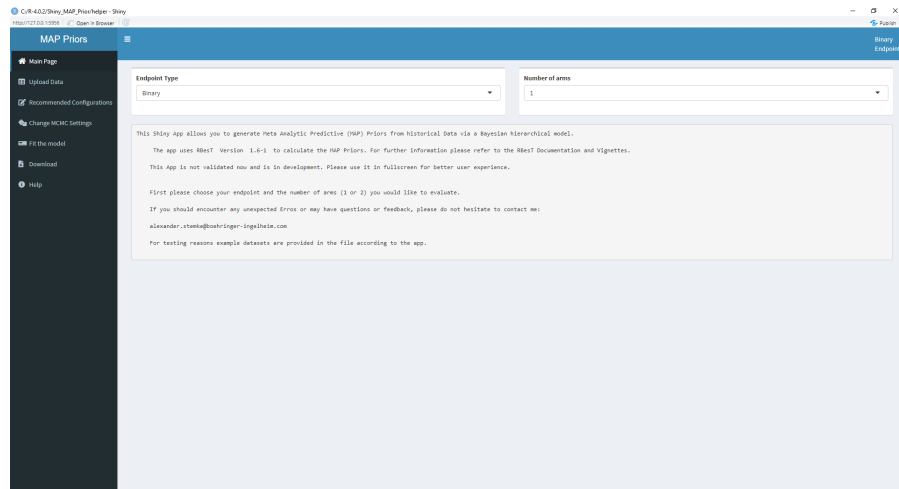


Figure 1: Main Page

The main page has mainly two essential inputs and some features.

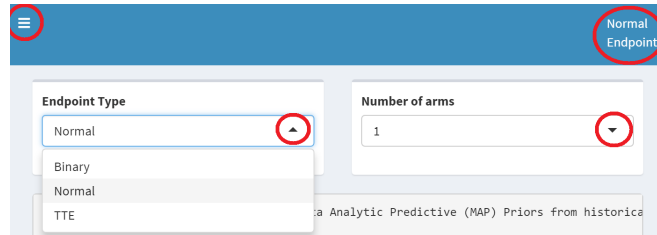


Figure 2: Main Page - Functions

The three lines let the sidebar collapse and expand. You can choose between 1 or 2 arms. The default is 1 arm. Each arm is represented by one dataset, the options for both datasets are equivalent. The priors will be fitted independently and make the use easier and faster. Under **Endpoint Type** you may choose between a binary, a normal or a time to event endpoint. The selected endpoint will be displayed in the upper right corner.

Depending on the choices the user interface may appear differently therefore the next chapter is structured regarding to the endpoint type.

All mandatory inputs have to be provided at the Main Page and the Upload tab. The model has to be fitted in the regarding tab and the results can be downloaded. Other tabs are optional and wherever possible default settings are provided.

3 Upload Data

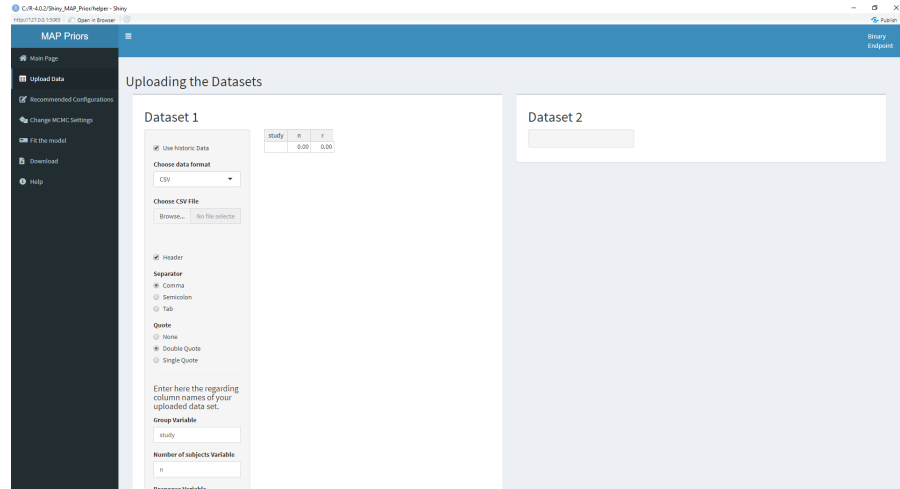


Figure 3: Upload Data

First of all there is the decision whether historical data shall be used (checkbox checked) or not. Following the further options will be explained.

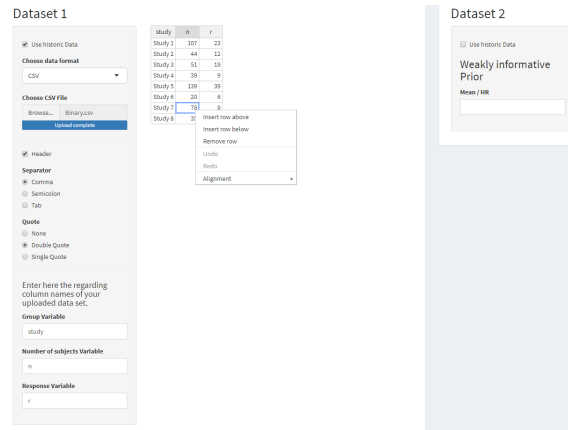


Figure 4: Uploaded Data

For historic studies one may either upload CSV or RDS files. Moreover the default setting and uploaded data can be treated like a Excel table. Every entry (except the header) can be edited and by a right click rows may be added or removed. You may also just type in the data without uploading anything.

Few parameter are obligatory to provide, if no historical data is provided. Which parameters these are depend on the chosen endpoint type.

The uploaded dataset can include more variables then necessary, following for each endpoint will be explained which variables have to be named.

Figure 5: Upload Files

You can upload CSV or RDS files. As CSV plain text and files with .csv are accepted. You can then configure whether a header is used, how the values are seperated and how the value are quoted. For a single R-Object it has to be saved as RDS and not as RDA to be uploaded.

3.1 Binary

Figure 6: Binary - variable names

For binary endpoints the dataset has to include the following variables:

Group variable - default: study

Number of subjects Variable - default: n

Response Variable - default: r

If your variables have different names, please change them according to your situation. Your dataset may include more variables but it has to include those three at least. In general r and n are whole numbers. If you have the response

rate, please calculate the number of responses.

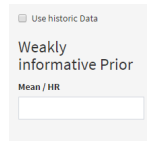


Figure 7: Binary without historical data

If no historic data is provided you have to give as input where you expect your mean/response to be around. Choose an integer between 0 and 1. The value 0.5 results in the uniform distribution.

3.2 Normal

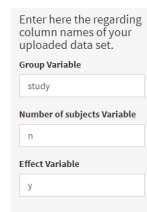


Figure 8: Normal - Variable names

Group variable - default: study

Number of subjects Variable - default: n

Effect Variable - default: y

If your variables have different names, please change them according to your situation. Your dataset may include more variables but it has to include those three at least. In general n is a whole number. And y is an integer according to the studies.

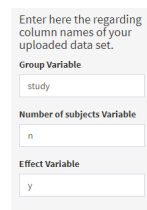
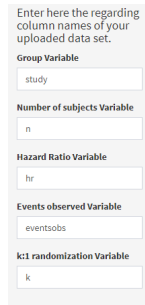


Figure 9: Normal without historical data

If no historic data is provided you have to give as input where you expect your mean to be around and what standard deviation your parameter would have.

3.3 TTE



Enter here the regarding column names of your uploaded data set.

Group Variable
study

Number of subjects Variable
n

Hazard Ratio Variable
hr

Events observed Variable
eventsobs

k:1 randomization Variable
k

Figure 10: TTE - variable names

Group variable - default: study

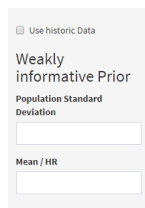
Number of subjects Variable - this variable is in this version of the app not relevant for TTE endpoints.

Hazard Ratio Variable - default: hr

Events observed Variable - default: eventsobs

k:1 randomization Variable - default: k

If your variables have different names, please change them according to your situation. Your dataset may include more variables but it has to include those four (excluding n) at least.



☐ Use historic Data

Weakly Informative Prior

Population Standard Deviation
[input field]

Mean / HR
[input field]

Figure 11: TTE without historic data

If no historic data is provided you have to give as input where you expect your Hazard Ratio to be around and what standard deviation your HR would have.

4 Recommended Configurations

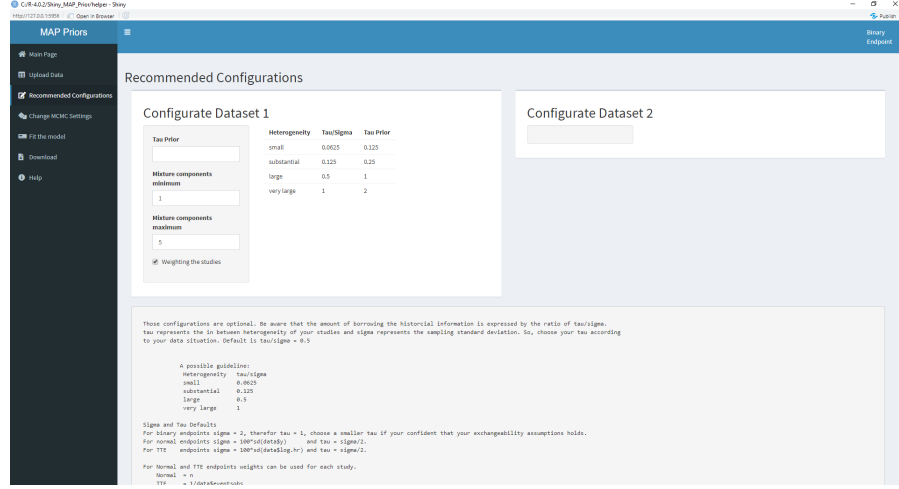


Figure 12: Recommended Configurations

Input at this tab is not necessary but can improve the model by a lot. For every possible input default settings exists. The most important input is the Tau Prior. The Tau Prior determines the amount of borrowing information from the historical data during the fitting. Smaller heterogeneity leads to more borrowing.

The table gives some guidance for possible Tau values. The default will be a large heterogeneity with $0.5 = \frac{\tau}{\sigma}$.

The defaults are

$$\begin{aligned} \sigma_{Binary} &= 2, \tau_{Binary} = 1, \\ \sigma_{Normal} &= 100 * sd(y), \tau_{normal} = \frac{\sigma_{Normal}}{2}, \\ \sigma_{TTE} &= 100 * sd(log(hr)), \tau_{TTE} = \frac{\sigma_{TTE}}{2}. \end{aligned}$$

4.1 Binary case

For binary input there are only options for the Tau prior. Smaller τ speaks for a smaller heterogeneity between the studies.

4.2 Normal and TTE case

An input for the population standard deviation will overwrite the default σ . If you have selected no historic information you have to provide your standard deviation again to get the table with recommendations.

Figure 13: Recommended Configurations

Figure 14: Recommended Configurations

5 Change MCMC Settings

Figure 15: Change MCMC settings

The MCMC Settings have mainly two components which are by default **not checked**. To make your results reproducible **check** the checkbox **Use Seed**.

Please keep in mind, that RBest uses Stan and therefor only results during the same session are reproduceable.

Moreover you can change the default MCMC settings, for more information please refer to further literature. If you change any settings you have to **check** the checkbox **Confirm to use personalized MCMC settings**.

Most warnings that occur during fitting, can be fixed by adjusting those settings, please refer to the guidance provided by the error.

6 Fit the model

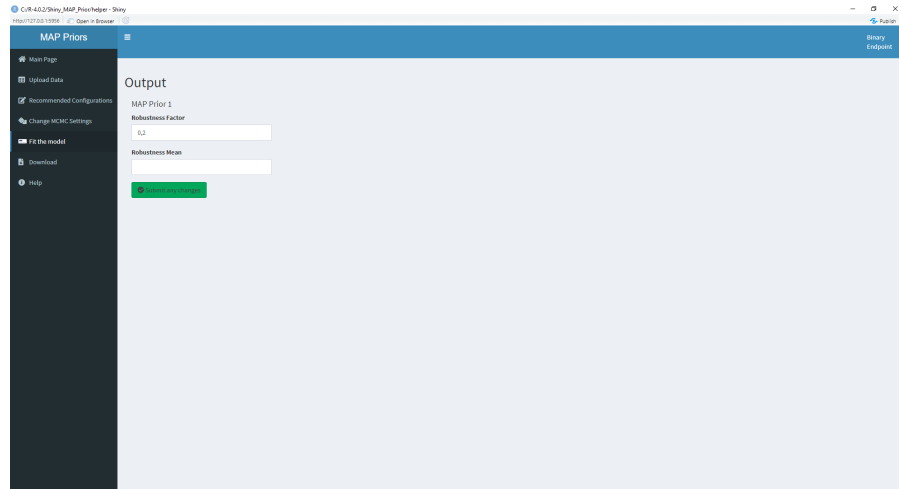


Figure 16: Fit the model

When you have done every necessary input you can press **Submit any changes** and your model will be fit. Depending on your hardware and moreover on your total iterations this process might take a while. While R is busy a loading screen is shown.

Moreover you are able to set the robustness factor and its mean. If you don't wish to include a robustification component, please set the **Robustness Factor** = 0.

To the left the model used historical data and therefore a forestplot is provided. To the right no historical data was provided. The bold black line is the predictive posterior. The colourful dashed lines are the components of the mixture distribution, which is also provided below the plot.

Output

MAP Prior 1

Robustness Factor

Robustness Mean

☒ Submit any changes




Figure 17: Loading screen

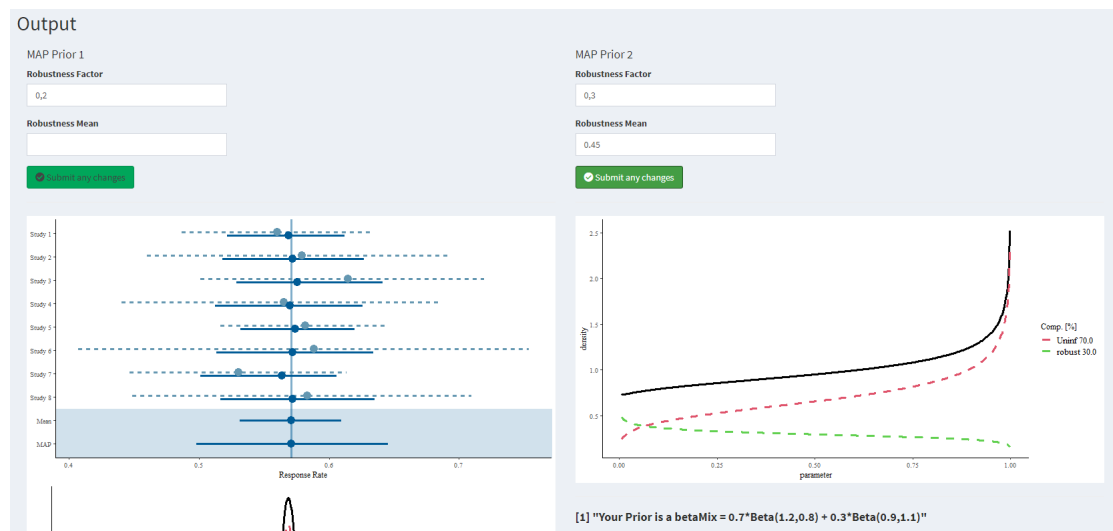


Figure 18: Fitted model

7 Download

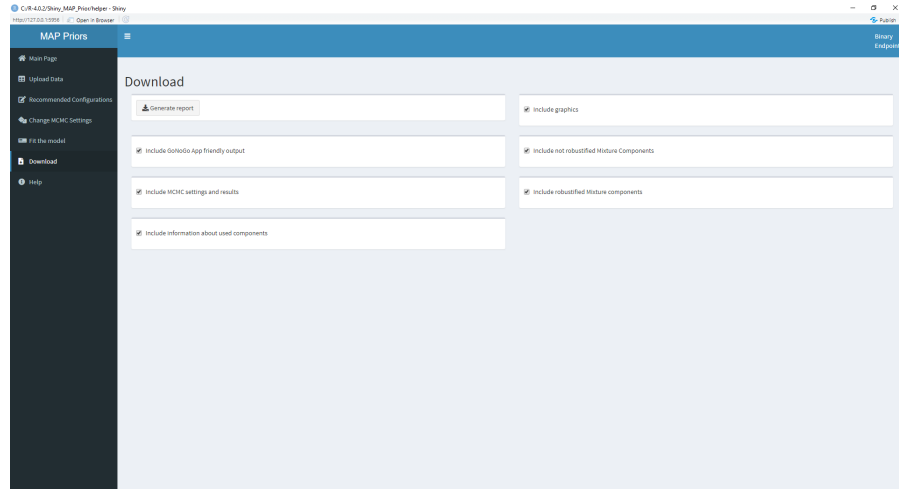


Figure 19: Download

In the download function every output is by default checked and will be included in a Word document, when **Generate report** is selected.

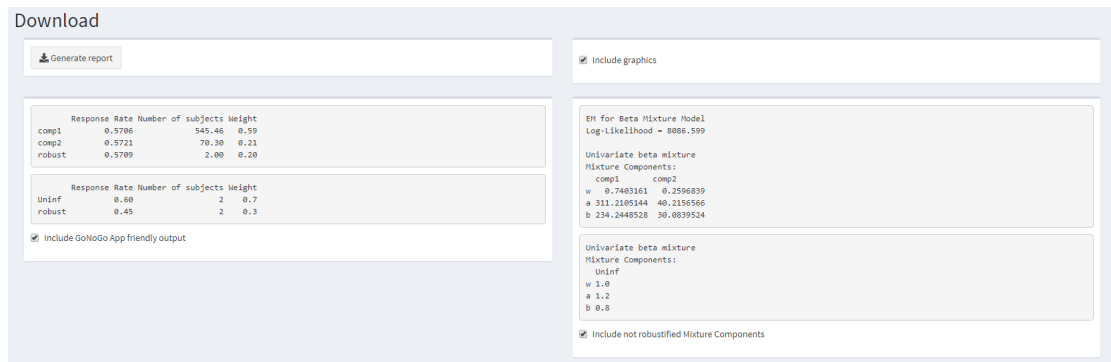


Figure 20: First Part - Download

Include graphics will include the mixture distribution and if available the forest plot.

Every row of **Include GoNoGo App friendly output** represents one component for the app. If less then four are displayed the remaining components have a weight of 0. The robust row counts as component as well.

Include not robustified Mixture components provides the Log-Likelihood for the mixture model, as well as the weights and parameters of the distribution.

X1

seed user_mcmc reprod warmup iter delta stepsize treedepth

1 1 -1224728992 FALSE FALSE 2000 6000 0.99 0.01 20

Generalized Meta Analytic Predictive Prior Analysis

Call: gMAP(formula = cbind(n, n - r) ~ 1 | study, family = binomial,
data = data, tau.dist = "halfNormal", tau.prior = config\$tau,
beta.prior = config\$sigma)

Exchangeability tau strata: 1
Prediction tau stratum : 1
Maximal lhat : 1

Between-trial heterogeneity of tau prediction stratum
mean sd 2.5% 50% 97.5%
0.09000 0.08130 0.00291 0.00000 0.30000

MAP Prior MCMC sample
mean sd 2.5% 50% 97.5%
0.5710 0.0349 0.4900 0.5710 0.6460

X2

seed user_mcmc reprod warmup iter delta stepsize treedepth

1 2 -1192826200 FALSE FALSE 2000 6000 0.99 0.01 20

NULL

☒ Include MCMC settings and results

Univariate beta mixture

Mixture Components:

comp1 comp2 robust
w 0.5922529 0.2077471 0.2000000
a 311.2105144 40.2196566 1.3418022
b 234.2440528 30.0839534 0.8581178

Univariate beta mixture

Mixture Components:

Uninf robust
w 0.7 0.3
a 1.2 0.9
b 0.8 1.1

☒ Include robustified Mixture components

X1 n_arms tau sigma rob rob_mean lhc_min lhc_max uninf_mean uninf_sigma

1 1 2 1 2 0.2 NA 1 5 NA NA

X1 r n endpoint_type historic study weight y hr k eventsobs

1 1 r n Binary TRUE study TRUE y hr k eventsobs

X2 n_arms tau sigma rob rob_mean lhc_min lhc_max uninf_mean uninf_sigma

1 2 2 1 2 0.2 NA 1 5 0.6 NA

X2 endpoint_type historic study weight n r y hr k eventsobs

1 2 Binary FALSE study TRUE n r y hr k eventsobs

☒ Include information about used components

Figure 21: Second Part - Download

Include MCMC settings and results provides the personalized or default settings and the characteristics of the MCMC sample.

Include robustified Mixture components provides the results which are plotted.

Include information about used components prints the input the server function uses for the gMAP call.

8 Common Errors

There are several errors that might occur. For severe warning a pop up will show up after the model is fitted. Please consider those warnings and try to eliminate them by following the advised steps.

Moreover in the report as well as below the mixture distribution, errors, warnings and messages are displayed.

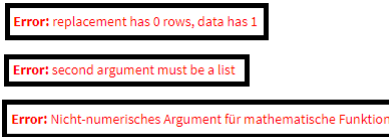


Figure 22: Error examples

A few errors also might occur while fitting the model, or during the recommendation table for τ . Please make sure that you have selected the correct endpoint and named your variables correctly.