

Probability of Success Using RBesT

RShiny App Walkthrough

James Normington

August 28, 2019

In this document, I briefly walk through a Shiny App to compute a trial's probability of success (PoS) using Sebastian Weber's RBesT package.

Compute MAP prior

The screenshot shows the 'Compute MAP prior' tab of the RBesT Shiny App. The interface includes a navigation bar with three tabs: 'Compute MAP prior' (active), 'PoS calculation', and 'Help'. The main content area is divided into two panels. The left panel contains two sections: (1) 'Choose endpoint type.' with a dropdown menu set to 'Binary' and a checked checkbox for 'Use historical trial meta-data'; and (2) 'Enter in historical meta-data.' with a sub-instruction 'Enter in data manually or upload .csv' and a dropdown menu set to 'Manual'. Below these is a table with three columns: 'Study', 'n at interim', and '# of events'. The table contains three rows of data. The right panel contains a single section: (4) 'Visualize meta-data and MAP prior.'.

Study	n at interim	# of events
Study 1	100	40
Study 2	100	50
Study 3	100	60

Use the first tab to specify the type of endpoint and whether or not your analysis should use historical data. If the *Use historical trial meta-data* box is checked, you can either edit the table directly or upload a .csv of data.

If you prefer to enter data into the table directly, check the *Add study to table?* checkbox, enter in the new information, and click *Add study* to add a study. To delete a study, use the *Delete study from table?* checkbox and specify the row you'd like to delete. If you choose to upload a .csv of data, change “Manual” to “Upload”. Ensure your data are in the format requested by the app, then use your computer browser to upload the file.

(3) Specify priors on τ and β .

Random seed (positive integer)

Specify prior for τ (between-trial standard deviation).

HalfNormal
▼

$\tau \sim \text{HalfNormal}(\sigma)$

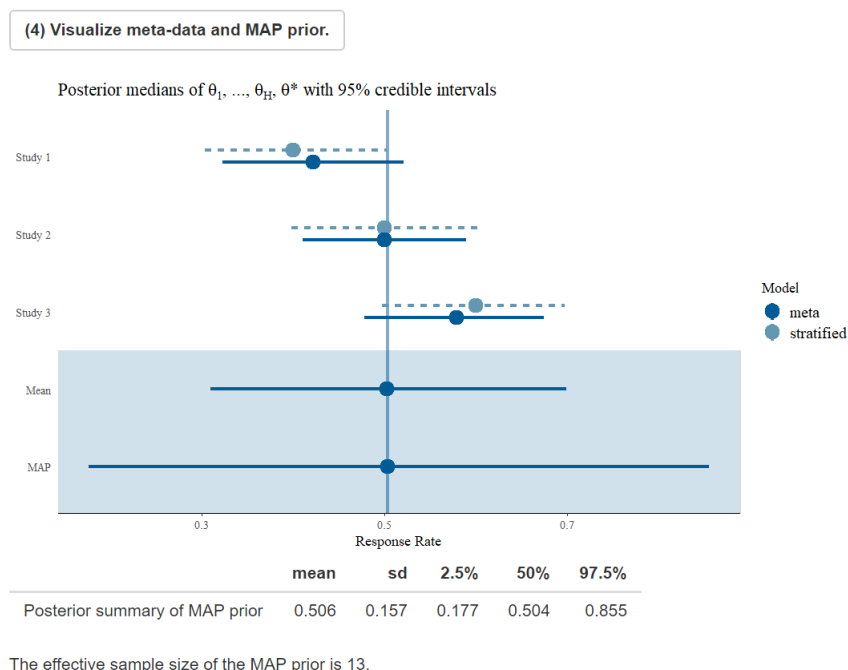
σ

Specify prior for β (common mean).

Default
▼

Default prior is $\beta \sim N(0, 2)$

Next, specify the random seed and hyper-priors on τ and β . A default prior for β will be suggested to you. To ignore this and specify a different prior for β , select “Specify” from the drop down and enter in the desired prior mean and standard deviation. A mean of 0 is recommended. The prior distribution on β must be Gaussian.



To create a forest plot to visualize the meta-data and MAP prior, click the (4) *Visualize MAP prior and compute ESS* button. To use an alternative method to compute ESS, change the *ESS method* input box. The author of this document strongly recommends using ELIR; see RBesT CRAN documentation for more details.

PoS calculation

Compute MAP prior

PoS calculation

Help

(1) Enter interim data.

One or two group trial?

One

☐ Concurrent trial data at interim?

Study	n at interim	# of events	# target patients
Study A	100	35	150

Weight for robust prior

0.2

Use the second tab to specify one- or two-group trial, the observed statistics at interim, as well as the total target sample size at the end of the trial. The table will dynamically

update as you toggle between “One” and “Two” groups and ☒ and ☐ in the *Concurrent trial data at interim?* box. The table is directly editable.

The code also automatically adds a robust component (e.g., a Uniform(0,1) for binary endpoints, a diffuse Gaussian distribution for Normal endpoints) to the prior mixture distributions. The default value is 0.2. To protect against an overly informative MAP prior, enter in a higher weight (say, 0.4). To allow the MAP prior to be more informative, enter in a lower weight (say, 0.1). It is not recommended to enter in a weight higher than 0.7.

(2) Enter the definition of trial success.

One or two success criteria?

Two

Lower or upper tail?

Upper

Decision rules:

(1) $P(p > p_0) > p_{crit}$

(2) $P(p > p_{02}) > p_{crit2}$

Null value, p_0

0.25

Critical probability threshold, p_{crit}

0.95

2nd null value, p_{02}

0.3

Critical probability threshold, p_{crit2}

0.5

(3) Compute PoS!

The probability of trial success is 0.957.

Use this section to specify the definition of trial success. You can specify one or two success criteria and a lower or upper tailed decision. As you toggle these options, the printed Decision rule(s) should dynamically update. If the trial has two groups, you can select a link function for the decision rule. For example, with binary endpoints, you can make a decision based on absolute difference in proportions (identity link), relative difference in odds (logit link), or relative difference in proportion (log link).

Enter in the null hypothesized values and critical probability threshold in accordance with the printed decision rule. Finally, click the (3) *Compute PoS!* button to compute the probability of trial success. If you are not using historical data, this should compute in less than a second. If you are using historical data but not analyzing a concurrent trial, this could take several seconds (though usually not more than one minute). If you are using historical data and using a concurrent trial, this may take a bit longer.