B-Safe Testing And Validation

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1 Background

The B-Safe r-shiny application is an interactive statistical software used to analyse several safety endpoints using the Bayesian (robust) Meta-Analytic Predictive (MAP) method. This approach was based on the works of [1].

1.1 Requirement Specification

The application will present it's results via graphs, tables and figures. The application will calculate the meta-analytic predictive (MAP) prior and the robust MAP priors, assesses prior data conflict and produces and effective sample size of the historical data.

The user will then be able to download output data/simulated results in a tabular form.

An error message is expected when the input table does not contain the required columns and when the input parameters does not match the intended analysis.

1.2 Purpose and Scope

The aim of this testing and validation plan is to test whether the application is working as specified and that all described functionality are working as intended.

Test cases will cover common use cases of the application with the aim of ensuring that calculations done by the application are implemented properly. If there are any computations that cannot be performed by the application, additional changes or modifications to the application will be done in the future. That is beyond the scope of this document.

2 Testing and Requirement Strategy

Software and packages used by the application to perform the validation includes:

Table 1: Softwares and Packages

Program	Version
R	
RStudio	
shiny	1.7.5.1
RBesT	1.7.2
Rmarkdown	2.25
R2jags	0.7-1
rstantools	2.1.1
bayesplot	1.8.1
checkmate	2.3.1
testthat	3.2.1

The testing strategy is based on Input Testing and Structural Testing. Input Testing is performed to investigate whether erroneous input by the user is handled as intended by the application. Structural Testing deals with the confirmation of the accuracy of the calculations done by the application. Different scenarios to cater for common cases will be simulated for the structural testing to be done.

3 Input Testing

This section describes the verification procedure of the functionality of the B-Safe application.

First, testing requirements and strategies are outlined. Then the handling of the testing failures and the processes for performing the testing are characterized.

The table below gives a brief overview about the parameters/variables the user is able to set as used within the document.

Table 2: Definitions of Variable

Variable	Description
STUDYID	Study number or name
HIST	0 for current trial and 1 for historical trial
ARM	Defines the treatment arm of the analysis
SAF_TOPIC	Safety topics of interest
N	Total number of patients in the respective study
N_WITH_AE	Total number of patients for the respective safety topic who expereienced at least one adverse event
TOT_EXP	Total exposure time for the respective safety topic: sum of patients treatment exposure period until occurence of first event. If no event occurs, use complete observation time
Dose	Amount/weight of the drug the patient took
Freq	Number of times in a day the medicine/drug was taken by the patient
Length	Number of days the patient was on the treatment
Treat	The specific treatment the patient was on
MAP Prior	Meta-Analytic Predictive Prior
CrI	Credible Interval
CrILB	Credible Interval Lower Boundary
CrIUB	Credible Interval Upper Boundary
ESS	Estimated Sample Size

In case the expected specifications are not met, the test is failed.

The conditions above are all implementations that needs to be tested before the actual testing of the full functionality of the Be-Safe application can be executed. Various test cases are grouped together and performed in a single action. For example, all test cases that contain checking the applications handling of input values/characters.

All those requirements are testest via the *checkmate* R package, which allows for both warnings as well as errors to guide the user along the error and help fixing the problem. In addition the required variables are within the same approach not only tested for specific required typing, but also the *checkmate* R package allows to test certain boundaries of those variables as well as restricting inputs to certain formats, e.g., csv.

3.1 Binary Endpoint

1. Uploaded file is a .csv file

Assumptions of the variables:

Table 3: Input

Input	Specification
File type	.csv file
STUDYID	character or numeric variable
HIST	boolean character variable
ARM	character variable
N	integer/numeric variable greater than zero
SAF_TOPIC	character variable with less than 30 characters
N_WITH_AE	integer variable greater than zero but less or equal to N
TOT_EXP	numeric varibale greater than zero
Dose	numeric variable that can be treated as a factor. It is an additional variable
Freq(Frequency)	integer variable that can be treated as a factor. It is an additional variable
Length	a numeric variable that is an additional factor

Robust MAP Prior:

2. Weakly-informative Prior weight is numeric between 0.01 and 0.99

New Trial Analysis:

3. Number of Patients in selected ARM is an integer > 0 but ≤ 200
4. Number of Patients with with AE is an integer ≥ 0 but $\leq$ number of patients in selected ARM

Decision Making:

5. Likelihood: Percentage of Patients with AE is an integer from 0 to 100
6. MAP Prior: Percentage of Patients with AE is an integer from 0 to 100
7. Robust MAP Prior: Percentage of Patients with AE is an integer from 0 to 100
8. Posterior: Percentage of Patients with AE is an integer from 0 to 100

Download Results:

9. Number of comparisons: integer from 1 to 5

Test cases were performed as shown in the the table below. Different formats of the various input are violated in different test cases. For any false input, the user shall be informed about the error and the error will be displayed and. The test is passed if no error message is displayed.

Test Case	Description of violation	Expected Response	Observed Response
1	An xlsx file uploaded	Error	Error
2	A file without the StudyID coulum uploaded	Error	Error
3	A file without the Hist coulum uploaded	Error	Error
4	A file without the ARM column uploaded	Error	Error
5	A file without N column uploaded	Error	Error
6	A file without N_WITH_AE uploaded	Error	Error
7	A file without SAF_Topic uploaded	Error	Error
8	A file without Dose column uploaded	No Error	No Error

Test Case	Description of violation	Expected Response	Observed Response
9	A file without FREQ column uploaded	No Error	No Error
10	A file without Length coumn uploaded	No Error	No Error
11	A file with number of Patients less than zero	Error	Error
12	A file with number of patients with AE greater than number of patients	Error	Error

Some inputs including weakly-informative prior weight for the calculation of Robust MAP Prior, number of patients in selected arm and number of patients with AE in the new trial analysis, percentages for making statistical inferences about MAP Prior, Robust MAP Prior, Likelihood and Posterior are all imputed with a slider. Different values along the range on the sliders will be tested in the various scenarios.

3.2 Time To Event Endpoint

1. Uploaded file is a .csv file

Assumptions of the variables:

Table 5: Input

Input	Specification
File type	.csv file
STUDYID	character or numeric variable
HIST	boolean character variable
ARM	character variable
N	integer/numeric variable greater than zero
SAF_TOPIC	character variable with less than 30 characters
N_WITH_AE	integer variable greater than zero but less or equal to N
TOT_EXP	numeric varibale greater than zero
Dose	numeric variable that can be treated as a factor. It is an additional variable
Freq(Frequency)	integer variable that can be treated as a factor. It is an additional variable
Length	a numeric variable that is an additional factor

Robust MAP Prior:

2. Weakly-informative Prior weight is numeric between 0.01 and 0.99
3. Weakly-informative Prior mean on the exp scale is numeric between 0.01 and 3

New Trial Analysis:

4. Number of first occurrence of the event is numeric between 1 and 200
5. Cumulative time to occurrence of the first events is numeric between 1 and 1000

Decision Making:

6. Likelihood: area of log(hazard) for patients with AE is numeric from 0.51 to 2.453
7. MAP Prior: area of log(hazard) for patients with AE is numeric from from 0.51 to 2.453
8. Robust MAP Prior: area of log(hazard) for patients with AE is numeric from from 0.51 to 2.453

9. Posterior: area of log(hazard) for patients with AE is numeric from from 0.51 to 2.453

Download Results:

10. Number of comparisons: integer from 1 to 5

Test Case	Description of violation	Expected Response	Observed Response
1	An xlsx file uploaded	Error	Error
2	A file without the StudyID coulum uploaded	Error	Error
3	A file without the Hist coulum uploaded	Error	Error
4	A file without the ARM column uploaded	Error	Error
5	A file without N column uploaded	Error	Error
6	A file without N_WITH_AE uploaded	Error	Error
7	A file without TOT_Exp uploaded	Error	Error
8	A file without SAF_Topic uploaded	Error	Error
9	A file without Dose column uploaded	No Error	No Error
10	A file without FREQ column uploaded	No Error	No Error
11	A file without Length coumn uploaded	No Error	No Error
12	A file with number of patients less than zero	Error	Error
13	A file with number of patients with AE greater than number of patients	Error	Error
14	A file with a negative TOT_Exp uploaded	Error	Error

Some inputs including weakly-informative prior weight for the calculation of Robust MAP Prior, number of patients in selected arm and number of patients with AE in the new trial analysis, percentages for making statistical inferences about MAP Prior, Robust MAP Prior, Likelihood and Posterior are all imputed with a slider. Different values along the range on the sliders will be tested in the various scenarios.

4 Testing Framework in testthat

To assure the testing of the thresholds for all the below defined scenarios as well as ensuring that the created plots do match saved up reference images for the same scenario, input parameters as well as seed. Therefore the *testthat* R package is being used to ensure a framework, that is commonly used and stable.

Hereby, the testing setup replicates partially the workflow of the application with loading the respective data, parameters as well as thresholds. Then all functions that B-SAFE is running are run in the needed order to ensure the same workflow. Afterwards the outputs of the different plots as well as tables that are being displayed within the application are compared against the reference images, where the binaries of the images are compared and expected to be equal. Regarding the tables, there thresholds, both for the lower as well as the upper limits are being used to create threshold tables which then the corresponding tables/values of the replicated application workflow are compared against. The framework then either passes the comparison as the values are equal within a certain tolerance e.g., 1e-03, or the framework will throw an error where this assumption is not met.

5 Scenario Testing - Description of Scenarios

Scenario testing was used to verify the computations the B-Safe Shiny application performs.

For this purpose, various conditions were set to capture a wide array of possibilities to set different parameter values. Each simulated scenario is a representation of a probable occurrence in a clinical trial. There are scenarios to cover heterogeneous and homogeneous data, very large to small borrowing of historical information, high and less robustification of the MAP prior. These scenarios are tested for both the Adverse Event Incidence Proportion and the Exposure-Adjusted Adverse Event Rate.

5.1 Adverse Event Incidence Proportion - Binary Endpoint

5.1.1 Scenario 1 - Best case Scenario

Scenario 1 describes a binary endpoint for a best case scenario where there was no censoring in the current trial, all events were observed during the trial, no noise in the data and homogeneous historical data. Input parameters are displayed in the table below:

Parameter	Input
Safety Analysis	Incidence Proportion
Safety Topic	Scen1
Between Trial Heterogeneity Prior Distribution	Half-Normal
Heterogeneity	Small
Effective Sample Size method	ELIR
tau/sigma	small
Robust weight	0.05
Number of patients with AE in Arm	194
Number of patients in Arm	200

5.1.2 Scenario 2 - Strong Prior Data Conflict

Scenario 2 describes a test case scenario for a binary endpoint with a strong prior data conflict between the historical and current trials. The characteristics of this scenario includes no censoring in the current trial, no noise, all events being observed, homogeneous historical data and hevay prior data conflict. Input parameters are displayed in the table below:

Parameter	Input
Safety Analysis	Incidence Proportion
Safety Topic	Scen2
Between Trial Heterogeneity Prior Distribution	Half-Normal
Heterogeneity	moderate
Effective Sample Size method	ELIR
tau/sigma	moderate
Robust weight	0.8
Number of patients with AE in Arm	199
Number of patients in Arm	200

5.1.3 Scenario 3 - Realistic Scenario

Scenario 3 describes a binary endpoint for a realistic situation with a dropout rate of 5%, some with a 2% tau, events observed at a 90% power, homogenous historical data and with no planned prior data conflict. Input parameters are displayed in the table below:

Parameter	Input
Safety Analysis	Incidence Proportion
Safety Topic	Scen3
Between Trial Heterogeneity Prior Distribution	Half-Normal
Heterogeneity	substantial
Effective Sample Size method	ELIR
tau/sigma	moderate
Robust weight	0.25
Number of patients with AE in Arm	31
Number of patients in Arm	200

5.1.4 Scenario 4 - Worst Case scenario

Scenario 4 describes a binary endpoint for a worst case scenario with huge censoring during the trial, huge noise in the data, low number of events observed at 90% power, heterogeneous historical data and huge data conflict. Input parameters are displayed in the table below:

Parameter	Input
Safety Analysis	Incidence Proportion
Safety Topic	Scen4
Between Trial Heterogeneity Prior Distribution	Half-Normal
Heterogeneity	very large
Effective Sample Size method	ELIR
tau/sigma	moderate
Robust weight	0.99
Number of patients with AE in Arm	27
Number of patients in Arm	50

5.1.5 Scenario 5 - Heterogeneous Data(Medium)

Scenario 5 describes a binary endpoint for a medium heterogenous scenario between the historical data, moderate noise at a 5% tau, moderate censoring at 5%, all events observed at a 90%power and no planned prior data conflict. Input parameters are displayed in the table below:

Parameter	Input
Safety Analysis	Incidence Proportion
Safety Topic	Scen5
Between Trial Heterogeneity Prior Distribution	Half-Normal
Heterogeneity	large
Effective Sample Size method	ELIR
tau/sigma	moderate
Robust weight	0.2
Number of patients with AE in Arm	25
Number of patients in Arm	200

5.1.6 Scenario 6 - High Dropout

Scenario 6 describes a binary endpoint scenario with huge dropout within the current trial, some noise at a 2% tau, some event being observed at a 90% power, homoenous data and no planned prior data conflict. Input parameters are displayed in the table below:

Parameter	Input
Safety Analysis	Incidence Proportion
Safety Topic	Scen6
Between Trial Heterogeneity Prior Distribution	Half-Normal
Heterogeneity	moderate
Effective Sample Size method	ELIR
tau/sigma	moderate
Robust weight	0.14
Number of patients with AE in Arm	31
Number of patients in Arm	200

5.1.7   Scenario 7- High Heterogeneous

Scenario 7 describes a binary endpoint scenario with high heterogeneity between historical data, moderate censoring in current trial, moderate noise at a 2% tau, all events observed at a 90% power, with no planned prior data conflict. Input parameters are displayed in the table below:

Parameter	Input
Safety Analysis	Incidence Proportion
Safety Topic	Scen7
Between Trial Heterogeneity Prior Distribution	Half-Normal
Heterogeneity	very large
Effective Sample Size method	ELIR
tau/sigma	very large
Robust weight	0.2
Number of patients with AE in Arm	35
Number of patients in Arm	200

5.1.8   Scenario 8 - Bad Scenario

Scenario 8 describes a binary endpoint for a bad scenario with huge censoring in the current trial, huge noise, little events observed in the current trial, heterogenous historical data and no planned prior data conflict. Input parameters are displayed in the table below:

Parameter	Input
Safety Analysis	Incidence Proportion
Safety Topic	Scen8
Between Trial Heterogeneity Prior Distribution	Half-Normal
Heterogeneity	large
Effective Sample Size method	ELIR
tau/sigma	large
Robust weight	0.2
Number of patients with AE in Arm	25
Number of patients in Arm	200

5.1.9   Scenario 9 - Good Scenario

Scenario 9 describes a binary endpoint for a good scenario with low censoring in the current trial,small noise, majority of the events being observed and homogeneous historical data. Input parameters are displayed in the table below:

Parameter	Input
Safety Analysis	Incidence Proportion
Safety Topic	Scen9
Between Trial Heterogeneity Prior Distribution	Half-Normal
Heterogeneity	moderate
Effective Sample Size method	ELIR
tau/sigma	large
Robust weight	0.05
Number of patients with AE in Arm	175
Number of patients in Arm	200

5.1.10 Scenario 10 - Favoured Control

Scenario 10 describes a binary endpoint for a favored control scenario with no censoring in the current trial, no noise, all events being observed, homogeneous historical data, heavy prior data conflict and the hazard ratio in favor of the control group. Input parameters are displayed in the table below:

Parameter	Input
Safety Analysis	Incidence Proportion
Safety Topic	Scen10
Between Trial Heterogeneity Prior Distribution	Half-Normal
Heterogeneity	small
Effective Sample Size method	ELIR
tau/sigma	small
Robust weight	0.05
Number of patients with AE in Arm	175
Number of patients in Arm	200

5.1.11 Scenario 11 - Continued study duration with Realistic Setting

Scenario 11 describes a binary endpoint for a realistic situation where the study continued regardless of when the proposed number of events has been observed. Characteristics of this scenario includes a droup out rate of 5%, noise at a 5% tau, homogenous historical data and no planned prior data conflict planned. Input parameters are displayed in the table below:

Parameter	Input
Safety Analysis	Incidence Proportion
Safety Topic	Scen11
Between Trial Heterogeneity Prior Distribution	Half-Normal
Heterogeneity	small
Effective Sample Size method	ELIR
tau/sigma	small
Robust weight	0.05
Number of patients with AE in Arm	170
Number of patients in Arm	200

5.1.12 Scenario 12 - Continued study duration with Worst Setting

Scenario 12 describes a binary endpoint for a scenario with a worst case scenario (scenario 4) that continued till the end of the proposed study duration. The scenario characteristics includes huge censoring, huge noise,

little events observed, heterogeneous historical and huge prior data conflict. Input parameters are displayed in the table below:

Parameter	Input
Safety Analysis	Incidence Proportion
Safety Topic	Scen12
Between Trial Heterogeneity Prior Distribution	Half-Normal
Heterogeneity	large
Effective Sample Size method	ELIR
tau/sigma	large
Robust weight	0.5
Number of patients with AE in Arm	30
Number of patients in Arm	200

5.1.13 Scenario 13 - High Dropout & too few people observed

Scenario 13 describes a binary endpoint for a situation with high dropout rate 0f 30%, small noise at a 2% tau, homogeneous historical data, few events being observed and no planned prior data conflict. Input parameters are displayed in the table below:

Parameter	Input
Safety Analysis	Incidence Proportion
Safety Topic	Scen13
Between Trial Heterogeneity Prior Distribution	Half-Normal
Heterogeneity	small
Effective Sample Size method	ELIR
tau/sigma	small
Robust weight	0.05
Number of patients with AE in Arm	15
Number of patients in Arm	200

5.2 Exposure-Adjusted Adverse Event Rate - Time To Event Endpoint

5.2.1 Scenario 1 - Best case scenario

Scenario 1 depicts a best case scenario for a time to event endpoint where there was no censoring, all events were observed during the trial, no noise in the data and the data was homogeneous amongst all historical trial. Input parameters are displayed in the table below:

Parameter	Input
Safety Anlysis	Exposure-adjusted AE rate
safety Topic	Scen1
Between trial heterogeneity distribution	Half-normal
Heterogeneity	small
ESS	ELIR
Robust weight	0.05
Exp mean	0.1
ESS method	ELIR
tau/sigma	small
Weakly-informative Prior weight	0.01

Parameter	Input
Weakly-informative Prior mean on the exp scale	0.1
Number of first occurrence of the event	100
Cummulative time to occurence of the first events	1000

5.2.2 Scenario 2 - Strong Prior Data Conflict

Scenario 2 describes a time to event test case scenario with a strong prior data conflict between the historical trials and the current trial. The characteristic of this scenario includes no censoring, no noise, all events being observed, homogeneous historical data and heavy prior data conflict. Input parameters are displayed in the table below:

Parameter	Input
Safety Anlysis	Exposure-adjusted AE rate
safety Topic	Scen2
Between trial heterogeneity distribution	Half-normal
Heterogeneity	moderate
ESS	ELIR
Robust weight	0.8
Exp mean	0.3854
ESS method	ELIR
tau/sigma	small
Weakly-informative Prior weight	0.8
Weakly-informative Prior mean on the exp scale	0.39
Number of first occurrence of the event	200
Cummulative time to occurence of the first events	518

5.2.3 Scenario 3 - Realistic Scenario

Scenario 3 describes a time to event endpoint for a realistic situation with a dropout rate of 5%, some noise with a tau of 2%, a 90% power, homogeneous historical data with no planned prior data conflict. Input parameters are displayed in the table below:

Parameter	Input
Safety Anlysis	Exposure-adjusted AE rate
safety Topic	Scen3
Between trial heterogeneity distribution	Half-normal
Heterogeneity	substantial
ESS	ELIR
Robust weight	0.25
Exp mean	0.0944
ESS method	ELIR
tau/sigma	small
Weakly-informative Prior weight	0.25
Weakly-informative Prior mean on the exp scale	0.09
Number of first occurrence of the event	31
Cummulative time to occurence of the first events	328

5.2.4 Scenario 4 - Worst case Scenario

Scenario 4 describes a time to event endpoint for a worst case scenario with huge censoring during the trial, huge noise, low number of events observed at a 90% power, heterogeneous historical data, and huge data conflict. Input parameters are displayed in the table below:

Parameter	Input
Safety Anlysis	Exposure-adjusted AE rate
safety Topic	Scen4
Between trial heterogeneity distribution	Half-normal
Heterogeneity	Very large
ESS	ELIR
Robust weight	0.99
Exp mean	0.0944
ESS method	ELIR
tau/sigma	small
Weakly-informative Prior weight	0.25
Weakly-informative Prior mean on the exp scale	0.05
Number of first occurrence of the event	31
Cummulative time to occurence of the first events	328

5.2.5 Scenario 5 - Heterogeneous Data(Medium)

Scenario 5 describes a time to event endpoint situation with medium heterogeneity between the historical data, moderate censoring at 5%, moderate noise with tau at 5%, all events observed with a power of 90% and no panned prior data conflict. Input parameters are displayed in the table below:

Parameter	Input
Safety Anlysis	Exposure-adjusted AE rate
safety Topic	Scen5
Between trial heterogeneity distribution	Half-normal
Heterogeneity	large
ESS	ELIR
Robust weight	0.2
Exp mean	0.0865
ESS method	ELIR
tau/sigma	small
Weakly-informative Prior weight	0.2
Weakly-informative Prior mean on the exp scale	0.09
Number of first occurrence of the event	25
Cummulative time to occurence of the first events	289

5.2.6 Scenario 6 - High Dropout

Scenario 6 describes a time to event endpoint situation with huge dropout within the current trial, some noise at a tau of 2", some events observed at a power of 90%, homogeneous data and no planned prior data conflict. Input parameters are displayed in the table below:

Parameter	Input
Safety Anlysis	Exposure-adjusted AE rate
safety Topic	Scen6
Between trial heterogeneity distribution	Half-normal
Heterogeneity	moderate
ESS	ELIR
Robust weight	0.14
Exp mean	0.1204
ESS method	ELIR
tau/sigma	small
Weakly-informative Prior weight	0.2
Weakly-informative Prior mean on the exp scale	0.12
Number of first occurrence of the event	31
Cummulative time to occurence of the first events	257

5.2.7 Scenario 7 - High heterogeneity

Scenario 7 describes a time to event endpoint situation with high heterogeneity between historical data, moderate censoring in current trial, moderate noise at tau of 2%, all events observed at a 90% power with no planned prior data conflict. Input parameters are displayed in the table below:

Parameter	Input
Safety Anlysis	Exposure-adjusted AE rate
safety Topic	Scen7
Between trial heterogeneity distribution	Half-normal
Heterogeneity	Very large
ESS	ELIR
Robust weight	0.2
Exp mean	0.186
ESS method	ELIR
tau/sigma	Very large
Weakly-informative Prior weight	0.2
Weakly-informative Prior mean on the exp scale	0.19
Number of first occurrence of the event	35
Cummulative time to occurence of the first events	200

5.2.8 Scenario 8 - Bad Scenario

Scenario 8 describes a time to event endpoint for a bad scenario with huge censoring in the current trial, huge noise, little events observed in the current trial, heterogeneous historical data and no planned prior data conflict. Input parameters are displayed in the table below:

Parameter	Input
Safety Anlysis	Exposure-adjusted AE rate
safety Topic	Scen8
Between trial heterogeneity distribution	Half-normal
Heterogeneity	large
ESS	ELIR
Robust weight	0.2
Exp mean	0.0741

Parameter	Input
ESS method	ELIR
tau/sigma	large
Weakly-informative Prior weight	0.2
Weakly-informative Prior mean on the exp scale	0.07
Number of first occurrence of the event	25
Cummulative time to occurence of the first events	338

5.2.9 Scenario 9 - Good Scenario

Scenario 9 describes a time to event endpoint for a good scenario with low censoring in the current trial, small noise, majority of the events being observed and homogeneous historical data. Input parameters are displayed in the table below:

Parameter	Input
Safety Anlysis	Exposure-adjusted AE rate
safety Topic	Scen9
Between trial heterogeneity distribution	Half-normal
Heterogeneity	small
ESS	ELIR
Robust weight	0.05
Exp mean	0.0926
ESS method	ELIR
tau/sigma	small
Weakly-informative Prior weight	0.05
Weakly-informative Prior mean on the exp scale	0.09
Number of first occurrence of the event	92
Cummulative time to occurence of the first events	1000

5.2.10 Scenario 10 - Favoured Control

Scenario 10 describes a time to event endpoint for a favored control scenario with no censoring in the current trial, no noise, all events being observed, homogeneous historical data, heavy prior data conflict and the hazard ratio in favor of the control group. Input parameters are displayed in the table below:

Parameter	Input
Safety Anlysis	Exposure-adjusted AE rate
safety Topic	Scen10
Between trial heterogeneity distribution	Half-normal
Heterogeneity	small
ESS	ELIR
Robust weight	0.6
Exp mean	0.2472
ESS method	ELIR
tau/sigma	small
Weakly-informative Prior weight	0.6
Weakly-informative Prior mean on the exp scale	1.2
Number of first occurrence of the event	150
Cummulative time to occurence of the first events	200

5.2.11 Scenario 11 - Continued study duration with Realistic Setting

Scenario 11 describes a time to event endpoint for a realistic situation where the study was continued regardless of when the proposed number of events has been observed. Characteristics of this scenario includes a dropout rate of 5%, noise at a tau of 25, homogeneous historical data and no planned prior data conflict. Input parameters are displayed in the table below:

Parameter	Input
Safety Anlysis	Exposure-adjusted AE rate
safety Topic	Scen11
Between trial heterogeneity distribution	Half-normal
Heterogeneity	small
ESS	ELIR
Robust weight	0.05
Exp mean	0.0952
ESS method	ELIR
tau/sigma	small
Weakly-informative Prior weight	0.05
Weakly-informative Prior mean on the exp scale	0.1
Number of first occurrence of the event	95
Cummulative time to occurence of the first events	1000

5.2.12 Scenario 12 - Continued study duration with Worst setting

Scenario 12 describes a binary endpoint for a scenario with a worst setting that continued till the end of the proposed study duration. The scenario characteristics includes huge censoring, huge noise, little events observed, heterogeneous historical and huge data conflict. Input parameters are displayed in the table below:

Parameter	Input
Safety Anlysis	Exposure-adjusted AE rate
safety Topic	Scen12
Between trial heterogeneity distribution	Half-normal
Heterogeneity	large
ESS	ELIR
Robust weight	0.2
Exp mean	0.2
ESS method	ELIR
tau/sigma	large
Weakly-informative Prior weight	0.5
Weakly-informative Prior mean on the exp scale	0.3
Number of first occurrence of the event	200
Cummulative time to occurence of the first events	1000

5.2.13 Scenario 13 - High Dropout & too few people observed

Scenario 13 describes a time to event endpoint for a situation with high dropout rate of 30%, small noise of tau at 2%, homogeneous historical, no planned prior data conflict and few events being observed. Input parameters are displayed in the table below:

Parameter	Input
Safety Anlysis	Exposure-adjusted AE rate
safety Topic	Scen13
Between trial heterogeneity distribution	Half-normal
Heterogeneity	small
ESS	ELIR
Robust weight	0.05
Exp mean	1.2
ESS method	ELIR
tau/sigma	small
Weakly-informative Prior weight	0.05
Weakly-informative Prior mean on the exp scale	1.2
Number of first occurrence of the event	71
Cummulative time to occurence of the first events	144

6 Simulation and Testing of Scenarios

In this chapter, the scenarios that were described in Chapter 3 will be simulated and run through the B-SAFE app with the results being cross-checked for errors.

First we simulate data accordingly to our specification. Then using the R-Script `ScriptThresholds.R` the lower and upper boundaries to be used for testing will be generated. This script does not use the functions of this package and calculates the values by using functions from `RBesT` and `base`. For this, each dataset of each scenario will go through 1.000 different analysis with different seeds. In consequence we take the minimum and the maximum of each parameter of interest.

It might happen, that during the testing we come across values greater or smaller those thresholds. The treshholds are displayed afterwards. During testing we include therefore a tolerance of $1 \ 10^{-4}$.

The scripts generates synthetic data that mimics real-world studies.

```
# Function to simulate 1 study
# nPat = Number of patients in each group
# g1 = group 1 (treatment); g2 = group 2 (control)
# dropout = 0_05: 5% dropout after time units of measure
# accr = accrual time, is to be in regards to the hazard
# NObsEvt = type 2 censoring, censor after NObsEvt number of events,
# probability of observing the event if < 1_
# accr_timepoint should include 0 and total accrual time_
# Pre-specify the censor type ahead of time


#' Simulate a study
#'
#' @param nPat
#' @param hz
#' @param dropout
#' @param accr
#' @param NObsEvt
#' @param accr_method
#' @param surv_method
#' @param intensity
#' @param accr_timepoint
```

```r
#' @param censor_type
#' @param time_cutoff
#'
#' @return
#' @export
#'
#' @examples
SimStudy <- function(nPat = c(g1 = 100, g2 = 100),
                     hz = c(g1 = 0.1, g2 = 0.2),
                     dropout = c(rate = 0.05, time = 12),
                     accr = 6,
                     NObsEvt = 0.5,
                     accr_method = "Uniform",
                     surv_method = "Exponential",
                     intensity = c(2, 6, 10),
                     accr_timepoint = c(0, 2, 4, 6),
                     censor_type = 1,
                     time_cutoff = 18) {
  N <- sum(nPat)
  # Observed events either proportional ( < 100) or as absolute numbers
  if (NObsEvt < 1) {
    NObsEvt <- sum(nPat) * NObsEvt
  }

  # res: variable which stores the result output
  # gID: 1 treatment 2 control
  # ID: Subject
  # Entry: Entry time according to accrual
  # EventTime: Simulated Eventtime + Entry time
  # ObsTime: Time observed (min(EventTime, CensorTime)-Entry)
  # StudyTime: Timepoint in Study
  # Eventindicator: 1 event observed, 0 censored
  res <- matrix(
    data = NA, nrow = N, ncol = 8,
    dimnames = list(
      ID = 1:N,
      c(
        "gID", "ID", "Entry", "EventTime",
        "ObsTime", "CensorTime",
        "StudyTime", "EventIndicator"
      )
    )
  )
  # ID and gID just from 1 to number of patients in each group
  res[, "ID"] <- 1:N
  res[, "gID"] <- c(rep(1, nPat["g1"]), rep(2, nPat["g2"]))

  # Different methods for generating Enrollment Time
  if (accr_method == "Uniform") {
    res[, "Entry"] <- runif(N, 0, accr)
  }

  # Poisson accrual times
```

```r
if (accr_method == "Poisson") {
  rtlist <- lapply(intensity, function(x) rexp(N, x))
  recruit_time <- c()
  for (i in 1:length(intensity)) {
    recruit_time_new <- c(accr_timepoint[i] +
      cumsum(rtlist[[i]][(accr_timepoint[i] +
        cumsum(rtlist[[i]])) < accr_timepoint[i + 1]]))
    recruit_time <- c(recruit_time, recruit_time_new)
  }
  if (length(recruit_time) < N) {
    enrollment <- c(recruit_time, runif(
      (N - length(recruit_time)),
      min(accr_timepoint), max(accr_timepoint)
    ))
  } else {
    enrollment <- recruit_time[1:N]
  }
  res[, "Entry"] <- enrollment
}

# Piecewise Uniform accrual times
if (accr_method == "Piecewise Uniform") {
  recruit_time <- c()
  for (i in 1:length(intensity)) {
    n_part <- intensity[i] * diff(accr_timepoint)[i]
    recruit_time_new <- runif(n_part, accr_timepoint[i], accr_timepoint[i + 1])
    recruit_time <- c(recruit_time, recruit_time_new)
  }
  if (length(recruit_time) < N) {
    enrollment <- c(recruit_time, runif(
      (N - length(recruit_time)),
      min(accr_timepoint),
      max(accr_timepoint)
    ))
  } else {
    enrollment <- recruit_time[1:N]
  }
  res[, "Entry"] <- enrollment
}

# Method for generating Survival Time
if (surv_method == "Exponential") {
  for (i in 1:length(nPat)) {
    SurvTimesG <- rexp(nPat[i], hz[i])
    if (i == 1) {
      SurvTimes <- SurvTimesG
    } else {
      SurvTimes <- c(SurvTimes, SurvTimesG)
    }
  }
}
```

```r
# Event Times
res[, "EventTime"] <- res[, "Entry"] + SurvTimes

# Get rate parameter for exponential distributed censoring times
CensorRate <- if (dropout["rate"] > 0) {
  -log(1 - dropout["rate"]) / dropout["time"]
} else {
  0
}

# Censoring times for all individuals, infinity if no censoring is applied
CensorTime <- if (dropout["rate"] > 0) {
  rexp(N, CensorRate)
} else {
  rep(Inf, N)
}

res[, "CensorTime"] <- CensorTime + res[, "Entry"]

# Censor type 1, administrative censoring after cutoff time
if (censor_type == 1) {
  evt_ind <- which(res[, "EventTime"] < res[, "CensorTime"] & res[, "EventTime"]
  < time_cutoff)
  non_evt_ind <- which(!(res[, "EventTime"] < res[, "CensorTime"] &
    res[, "EventTime"] < time_cutoff))
  res[evt_ind, "EventIndicator"] <- 1
  res[non_evt_ind, "EventIndicator"] <- 0
  res[evt_ind, "ObsTime"] <- res[evt_ind, "EventTime"] - res[evt_ind, "Entry"]
  res[non_evt_ind, "ObsTime"] <- ifelse(res[non_evt_ind, "CensorTime"] <
    time_cutoff,
  res[non_evt_ind, "CensorTime"] -
    res[non_evt_ind, "Entry"],
  time_cutoff - res[non_evt_ind, "Entry"]
  )
  res[, "StudyTime"] <- res[, "ObsTime"] + res[, "Entry"]
}


# Type 2 censoring, censoring after number of observed events
if (censor_type == 2) {
  # Introduce censoring indices
  evt_ind <- which(res[, "EventTime"] < res[, "CensorTime"])
  non_evt_ind <- which(res[, "EventTime"] >= res[, "CensorTime"])
  res[evt_ind, "EventIndicator"] <- 1
  res[non_evt_ind, "EventIndicator"] <- 0
  res[evt_ind, "ObsTime"] <- res[evt_ind, "EventTime"] - res[evt_ind, "Entry"]
  res[non_evt_ind, "ObsTime"] <- res[non_evt_ind, "CensorTime"] -
    res[non_evt_ind, "Entry"]
  res[, "StudyTime"] <- res[, "ObsTime"] + res[, "Entry"]

  type2_censortime <- sort(res[, "StudyTime"], decreasing = FALSE)[NObsEvt]
  type2_censorind <- which(res[, "StudyTime"] > type2_censortime)
  res[type2_censorind, "StudyTime"] <- type2_censortime
```

```r
    res[type2_censorind, "EventIndicator"] <- 0

    new_censored_row_idx <- which(res[, "StudyTime"] == type2_censortime)

    res[new_censored_row_idx, "ObsTime"] <- type2_censortime -
      res[new_censored_row_idx, "Entry"]
  }

  res <- as.data.frame(res)
  return(res)
}
```

The data set that will be used for testing the various scenarios is then simulate using scenario specific variables.

```r
#' Simulate Test Data Set
#'
#' @param SimStudy_nPat
#' @param SimStudy_hz
#' @param SimStudy_dropout
#' @param SimStudy_accr
#' @param SimStudy_accr_method
#' @param SimStudy_surv_method
#' @param SimStudy_intensity
#' @param SimStudy_accr_timepoint
#' @param SimStudy_time_cutoff
#' @param SimStudy_NObsEvt
#' @param SimStudy_censor_type
#' @param nStudy Number
#' @param tau
#' @param prior_data_conflict
#' @param SAF_TOPIC
#' @param pdc_hz
#'
#' @return
#' @export
#'
#' @examples
SimTestData <- function(
    SimStudy_nPat = c(g1 = 50, g2 = 100),
    SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
    SimStudy_dropout = c(rate = 0.05, time = 18),
    SimStudy_accr = 6,
    SimStudy_accr_method = "Uniform",
    SimStudy_surv_method = "Exponential",
    SimStudy_intensity = c(2, 4, 6),
    SimStudy_accr_timepoint = c(0, 2, 4, 6),
    SimStudy_time_cutoff = 18,
    SimStudy_NObsEvt = 100,
    SimStudy_censor_type = 1,
    nStudy = 5,
    tau = 0,
    prior_data_conflict = FALSE,
```

```
    pdc_hz = c(g1 = 0.05, g2 = 0.5),
    SAF_TOPIC = "Example",
    seed = 123) {
res <- array(
  data = NA, dim = c(nStudy, 5, 2),
  dimnames = list(
    STUDYID = c(1:nStudy),
    c("HIST", "ARM", "N", "N_WITH_AE", "TOT_EXP"),
    c("g1", "g2")
  )
)

res[1:(nStudy - 1), "HIST", ] <- 1
res[nStudy, "HIST", ] <- 0

res[, "ARM", "g1"] <- 1
res[, "ARM", "g2"] <- 2

res[, "N", "g1"] <- SimStudy_nPat["g1"]
res[, "N", "g2"] <- SimStudy_nPat["g2"]

# intiualize the list to save the data
res_SimStudy <- list()

#
if (!is.na(seed)) {
  set.seed(seed)
}

# For prior Data conflict, simulate n-1 similar and 1 different trial
if (prior_data_conflict == TRUE) {
  nStudy <- nStudy - 1
}

# Simulate sutdies
for (i in 1:nStudy) {
  if (tau > 0) {
    SimStudy_hz <- exp(log(SimStudy_hz) + rnorm(2, mean = 0, sd = tau))
  }
  res_SimStudy[[i]] <- SimStudy(
    nPat = SimStudy_nPat,
    hz = SimStudy_hz,
    dropout = SimStudy_dropout,
    accr = SimStudy_accr,
    accr_method = SimStudy_accr_method,
    surv_method = SimStudy_surv_method,
    intensity = SimStudy_intensity,
    accr_timepoint = SimStudy_accr_timepoint,
    time_cutoff = SimStudy_time_cutoff,
    NObsEvt = SimStudy_NObsEvt,
    censor_type = SimStudy_censor_type
  )
}
```

```r
  # Simulate the different trial
  if (prior_data_conflict == TRUE) {
    nStudy <- nStudy + 1

    res_SimStudy[[nStudy]] <- SimStudy(
      nPat = SimStudy_nPat,
      hz = pdc_hz,
      dropout = SimStudy_dropout,
      accr = SimStudy_accr,
      accr_method = SimStudy_accr_method,
      surv_method = SimStudy_surv_method,
      intensity = SimStudy_intensity,
      accr_timepoint = SimStudy_accr_timepoint,
      time_cutoff = SimStudy_time_cutoff,
      NObsEvt = SimStudy_NObsEvt,
      censor_type = SimStudy_censor_type
    )
  }

  for (s in 1:nStudy) {
    for (g in 1:2) {
      res[s, "TOT_EXP", g] <-
        sum(res_SimStudy[[s]][res_SimStudy[[s]]$gID == g, ]$ObsTime)

      res[s, "N_WITH_AE", g] <-
        sum(res_SimStudy[[s]][res_SimStudy[[s]]$gID == g, ]$EventIndicator)
    }
  }

  res_df <- as.data.frame(rbind(res[, , 1], res[, , 2]))
  row.names(res_df) <- c(paste0(c(1:nStudy), "_g1"), paste0(c(1:nStudy), "_g2"))
  res_df$STUDYID <- c(paste0("Study#", 1:nStudy), paste0("Study#", 1:nStudy))
  res_df[res_df$ARM == 1, "ARM"] <- "g1"
  res_df[res_df$ARM == 2, "ARM"] <- "g2"
  res_df$SAF_TOPIC <- SAF_TOPIC
  res_df <- res_df[, c(
    "STUDYID", "HIST", "ARM", "N",
    "SAF_TOPIC", "N_WITH_AE", "TOT_EXP"
  )]
  res_df$DOSE <- 999
  res_df$FREQ <- 999
  res_df$LENGTH <- 999
  res_df$TREAT <- SAF_TOPIC

  return(res_df)
}
```

6.1 Binary Endpoint

6.1.1 Scenario 1 - Best Case Scenario

```
# Scen1
SimTestData(
  SimStudy_nPat = c(g1 = 300, g2 = 300),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0, time = 12),
  SimStudy_accr = 1,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 0.999,
  SimStudy_censor_type = 2,
  nStudy = 10,
  tau = 0,
  prior_data_conflict = FALSE,
  pdc_hz = NA,
  SAF_TOPIC = "Scen1",
  seed = 1699874539
)
```

```
##          STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE  TOT_EXP DOSE FREQ LENGTH TREAT
## 1_g1    Study#1    1  g1 300     Scen1       299 2828.715  999  999    999 Scen1
## 2_g1    Study#2    1  g1 300     Scen1       299 2882.367  999  999    999 Scen1
## 3_g1    Study#3    1  g1 300     Scen1       299 3236.408  999  999    999 Scen1
## 4_g1    Study#4    1  g1 300     Scen1       299 3085.252  999  999    999 Scen1
## 5_g1    Study#5    1  g1 300     Scen1       299 2984.353  999  999    999 Scen1
## 6_g1    Study#6    1  g1 300     Scen1       299 3305.953  999  999    999 Scen1
## 7_g1    Study#7    1  g1 300     Scen1       299 2975.530  999  999    999 Scen1
## 8_g1    Study#8    1  g1 300     Scen1       299 3103.969  999  999    999 Scen1
## 9_g1    Study#9    1  g1 300     Scen1       299 2763.876  999  999    999 Scen1
## 10_g1 Study#10    0  g1 300     Scen1       299 3044.691  999  999    999 Scen1
## 1_g2    Study#1    1  g2 300     Scen1       300 1466.836  999  999    999 Scen1
## 2_g2    Study#2    1  g2 300     Scen1       300 1604.556  999  999    999 Scen1
## 3_g2    Study#3    1  g2 300     Scen1       300 1428.295  999  999    999 Scen1
## 4_g2    Study#4    1  g2 300     Scen1       300 1472.222  999  999    999 Scen1
## 5_g2    Study#5    1  g2 300     Scen1       300 1678.517  999  999    999 Scen1
## 6_g2    Study#6    1  g2 300     Scen1       300 1504.812  999  999    999 Scen1
## 7_g2    Study#7    1  g2 300     Scen1       300 1626.479  999  999    999 Scen1
## 8_g2    Study#8    1  g2 300     Scen1       300 1480.283  999  999    999 Scen1
## 9_g2    Study#9    1  g2 300     Scen1       300 1644.251  999  999    999 Scen1
## 10_g2 Study#10    0  g2 300     Scen1       300 1519.465  999  999    999 Scen1
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                            csv group          analysis saf_topic      seed
```

```
## Best case scenario scen01.csv    g1 Incidence proportion    Scen01 1699874539
##                    pool      tau heterog  ESS rob_weight nta_event nta_npat
## Best case scenario TRUE HalfNormal   Small elir      0.05      194      200
```

Characteristic	Lower Threshold	Upper Threshold
Expected MAP Prior: mean	0.979491547394171	0.979783497956057
Expected MAP Prior: SD	0.00285202608365105	0.00351178374809926
Expected MAP Prior: median	0.979607035575529	0.979971824880252
95% CrILB	0.971672478825027	0.973764750983234
95% CrIUB	0.984656603290914	0.985656486594363
ESS	1793.88265700888	2552.32572379732
Expected robustified MAP Prior: mean	0.955517010507768	0.955794315167282
Expected robustified MAP Prior: SD	0.122865418944131	0.122918290913021
Expected robustified MAP Prior: median	0.979403967044861	0.979764840500415
95% CrILB	0.5	0.5
95% CrIUB	0.98468573652361	0.985610481567658
ESS	1695.30906525778	2410.04506994399
Expected results for Likelihood: mean	0.97	0.97
Expected results for Likelihood: SD	0.0120322948518976	0.0120322948518976
Expected results for Likelihood: median	0.97155465341774	0.97155465341774
95% CrILB	0.942342194177027	0.942342194177027
95% CrIUB	0.988856429616452	0.988856429616452
ESS	NA	NA
Expected results for Posterior: mean	0.978524406955921	0.978981290460374
Expected results for Posterior: SD	0.00295019107632783	0.003590937771249
Expected results for Posterior: median	0.978834744477407	0.979191423833967
95% CrILB	0.970301812787683	0.972906006557673
95% CrIUB	0.983945205181107	0.984381528954003
ESS	NA	NA

6.1.2 Scenario 2 - Strong Prior Data Conflict

Scenario 2 describes a test case scenario for a binary endpoint with a strong prior data conflict between the historical and current trials. The characteristics of this scenario includes no censoring in the current trial, no noise, all events being observed, homogeneous historical data and heavy prior data conflict.

```
# Scen2
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.3),
  SimStudy_dropout = c(rate = 0, time = 12),
  SimStudy_accr = 1,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 0.9,
  SimStudy_censor_type = 2,
  nStudy = 10,
  tau = 0.01,
  prior_data_conflict = TRUE,
```

```
  pdc_hz = c(g1 = 0.4, g2 = 0.05),
  SAF_TOPIC = "Scen2",
  seed = 1701611344
)
```

```
##          STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE   TOT_EXP DOSE FREQ LENGTH
## 1_g1    Study#1    1  g1 200     Scen2       161 1530.2128  999  999    999
## 2_g1    Study#2    1  g1 200     Scen2       162 1528.7454  999  999    999
## 3_g1    Study#3    1  g1 200     Scen2       160 1660.3443  999  999    999
## 4_g1    Study#4    1  g1 200     Scen2       161 1840.7538  999  999    999
## 5_g1    Study#5    1  g1 200     Scen2       162 1605.1504  999  999    999
## 6_g1    Study#6    1  g1 200     Scen2       164 1496.5477  999  999    999
## 7_g1    Study#7    1  g1 200     Scen2       161 1622.6838  999  999    999
## 8_g1    Study#8    1  g1 200     Scen2       162 1575.8092  999  999    999
## 9_g1    Study#9    1  g1 200     Scen2       161 1638.6499  999  999    999
## 10_g1 Study#10    0  g1 200     Scen2       200  439.5240  999  999    999
## 1_g2    Study#1    1  g2 200     Scen2       199  723.4652  999  999    999
## 2_g2    Study#2    1  g2 200     Scen2       198  725.3088  999  999    999
## 3_g2    Study#3    1  g2 200     Scen2       200  633.6027  999  999    999
## 4_g2    Study#4    1  g2 200     Scen2       199  631.2705  999  999    999
## 5_g2    Study#5    1  g2 200     Scen2       198  701.9784  999  999    999
## 6_g2    Study#6    1  g2 200     Scen2       196  705.4184  999  999    999
## 7_g2    Study#7    1  g2 200     Scen2       199  680.0606  999  999    999
## 8_g2    Study#8    1  g2 200     Scen2       198  704.2055  999  999    999
## 9_g2    Study#9    1  g2 200     Scen2       199  727.2699  999  999    999
## 10_g2 Study#10    0  g2 200     Scen2       160 3910.1011  999  999    999
##         TREAT
## 1_g1    Scen2
## 2_g1    Scen2
## 3_g1    Scen2
## 4_g1    Scen2
## 5_g1    Scen2
## 6_g1    Scen2
## 7_g1    Scen2
## 8_g1    Scen2
## 9_g1    Scen2
## 10_g1 Scen2
## 1_g2    Scen2
## 2_g2    Scen2
## 3_g2    Scen2
## 4_g2    Scen2
## 5_g2    Scen2
## 6_g2    Scen2
## 7_g2    Scen2
## 8_g2    Scen2
## 9_g2    Scen2
## 10_g2 Scen2
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                                 csv group           analysis saf_topic
```

```
## Strong Prior Data Conflict Scen02.csv    g1 Incidence proportion    Scen02
##                                seed pool       tau  heterog  ESS rob_weight
## Strong Prior Data Conflict 1701611344 TRUE HalfNormal Moderate elir      0.8
##                          nta_event nta_npat
## Strong Prior Data Conflict       199      200
```

Characteristic	Lower Threshold	Upper Threshold
Expected MAP Prior: mean	0.806863934257434	0.808201537976221
Expected MAP Prior: SD	0.0115551278259737	0.0157011780943237
Expected MAP Prior: median	0.807028236716323	0.808486332610378
95% CrILB	0.773105540092442	0.784828744212647
95% CrIUB	0.828447898577212	0.836306179633206
ESS	809.812481460494	1246.60774990097
Expected robustified MAP Prior: mean	0.561372762043643	0.561640286682186
Expected robustified MAP Prior: SD	0.28594043560982	0.286168338911805
Expected robustified MAP Prior: median	0.62498071206025	0.624999868900733
95% CrILB	0.0312378996607603	0.0312378996607603
95% CrIUB	0.96876210033924	0.96876210033924
ESS	111.137253380954	174.019577068194
Expected results for Likelihood: mean	0.995	0.995
Expected results for Likelihood: SD	0.00497506218866618	0.00497506218866618
Expected results for Likelihood: median	0.996522907474637	0.996522907474637
95% CrILB	0.981633672305585	0.981633672305585
95% CrIUB	0.999872782927028	0.999872782927028
ESS	NA	NA
Expected results for Posterior: mean	0.990099009899753	0.990099009900987
Expected results for Posterior: SD	0.00694913273605492	0.00694913274503791
Expected results for Posterior: median	0.991645917011147	0.991651167327831
95% CrILB	0.972587345987852	0.972616880820979
95% CrIUB	0.998762474433972	0.998823508949902
ESS	NA	NA

6.1.3 Scenario 3 - Realistic Scenario

Scenario 3 describes a binary endpoint for a realistic situation with a dropout rate of 5%, some with a 2% tau, events observed at a 90% power, homogeneous historical data and with no planned prior data conflict.

```
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0.05, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 93,
  SimStudy_censor_type = 2,
  nStudy = 6,
  tau = 0.02,
```

```
  prior_data_conflict = FALSE,
  pdc_hz = NA,
  SAF_TOPIC = "Scen3",
  seed = 1701621384
)
```

```
##       STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE  TOT_EXP DOSE FREQ LENGTH TREAT
## 1_g1 Study#1    1  g1 200     Scen3        30 282.8273  999  999    999 Scen3
## 2_g1 Study#2    1  g1 200     Scen3        35 345.5776  999  999    999 Scen3
## 3_g1 Study#3    1  g1 200     Scen3        32 355.6786  999  999    999 Scen3
## 4_g1 Study#4    1  g1 200     Scen3        35 409.5392  999  999    999 Scen3
## 5_g1 Study#5    1  g1 200     Scen3        36 207.1725  999  999    999 Scen3
## 6_g1 Study#6    0  g1 200     Scen3        40 291.3027  999  999    999 Scen3
## 1_g2 Study#1    1  g2 200     Scen3        60 259.6821  999  999    999 Scen3
## 2_g2 Study#2    1  g2 200     Scen3        52 268.0612  999  999    999 Scen3
## 3_g2 Study#3    1  g2 200     Scen3        57 237.5458  999  999    999 Scen3
## 4_g2 Study#4    1  g2 200     Scen3        54 359.4474  999  999    999 Scen3
## 5_g2 Study#5    1  g2 200     Scen3        52 170.1687  999  999    999 Scen3
## 6_g2 Study#6    0  g2 200     Scen3        50 266.0703  999  999    999 Scen3
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                               csv group          analysis saf_topic      seed
## Realisitic Scenarios Scen03.csv    g1 Incidence proportion    Scen03 1701621384
##                       pool       tau     heterog  ESS rob_weight nta_event
## Realisitic Scenarios TRUE HalfNormal Substantial elir       0.25        31
##                      nta_npat
## Realisitic Scenarios      200
```

Characteristic	Lower Threshold	Upper Threshold
Expected MAP Prior: mean	0.171112086574982	0.174801757383778
Expected MAP Prior: SD	0.0312981929542034	0.0460599248842795
Expected MAP Prior: median	0.169358359437579	0.17204272796414
95% CrILB	0.0948197686428197	0.11714670059535
95% CrIUB	0.240651246385122	0.289617261629821
ESS	141.880220661842	225.148725074059
Expected robustified MAP Prior: mean	0.253324197751636	0.256104005534175
Expected robustified MAP Prior: SD	0.203829310436031	0.205771870157893
Expected robustified MAP Prior: median	0.176112724735265	0.178825854001896
95% CrILB	0.0733618511785474	0.0890733542137381
95% CrIUB	0.90000000076795	0.900027320591585
ESS	97.4735633197327	155.747670250313
Expected results for Likelihood: mean	0.155	0.155
Expected results for Likelihood: SD	0.0255267881924633	0.0255267881924633
Expected results for Likelihood: median	0.153848972465443	0.153848972465443
95% CrILB	0.108364536862043	0.108364536862043
95% CrIUB	0.208163854001394	0.208163854001394
ESS	NA	NA
Expected results for Posterior: mean	0.162632517373771	0.164596299739323

Characteristic	Lower Threshold	Upper Threshold
Expected results for Posterior: SD	0.0176283854694983	0.0191746642207218
Expected results for Posterior: median	0.16271459627216	0.164954956125394
95% CrILB	0.124303395032331	0.129607611354869
95% CrIUB	0.197774732106609	0.200472100086111
ESS	NA	NA

6.1.4 Scenario 4 - Worst Case Scenario

Scenario 4 describes a binary endpoint for a worst case scenario with huge censoring during the trial, huge noise in the data, low number of events observed at 90% power, heterogeneous historical data and huge data conflict.

```
SimTestData(
  SimStudy_nPat = c(g1 = 50, g2 = 100),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0.2, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 112,
  SimStudy_censor_type = 2,
  nStudy = 3,
  tau = 0.15,
  prior_data_conflict = TRUE,
  pdc_hz = c(g1 = 0.05, g2 = 0.1),
  SAF_TOPIC = "Scen4",
  seed = 1701626683
)
```

```
##        STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE  TOT_EXP DOSE FREQ LENGTH TREAT
## 1_g1 Study#1    1  g1  50     Scen4        28 197.5691  999  999    999 Scen4
## 2_g1 Study#2    1  g1  50     Scen4        27 237.3923  999  999    999 Scen4
## 3_g1 Study#3    0  g1  50     Scen4        23 425.0280  999  999    999 Scen4
## 1_g2 Study#1    1  g2 100     Scen4        73 283.1671  999  999    999 Scen4
## 2_g2 Study#2    1  g2 100     Scen4        73 334.8827  999  999    999 Scen4
## 3_g2 Study#3    0  g2 100     Scen4        70 750.5857  999  999    999 Scen4
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                          csv group            analysis saf_topic       seed
## Worst Case Scenario Scen04.csv   g1 Incidence proportion    Scen04 1701626683
##                    pool     tau    heterog  ESS rob_weight nta_event
## Worst Case Scenario TRUE HalfNormal Very Large elir       0.99        27
##                    nta_npat
## Worst Case Scenario      50
```

Characteristic	Lower Threshold	Upper Threshold
Expected MAP Prior: mean	NA	NA
Expected MAP Prior: SD	NA	NA
Expected MAP Prior: median	NA	NA
95% CrILB	NA	NA
95% CrIUB	NA	NA
ESS	NA	NA
Expected robustified MAP Prior: mean	NA	NA
Expected robustified MAP Prior: SD	NA	NA
Expected robustified MAP Prior: median	NA	NA
95% CrILB	NA	NA
95% CrIUB	NA	NA
ESS	NA	NA
Expected results for Likelihood: mean	NA	NA
Expected results for Likelihood: SD	NA	NA
Expected results for Likelihood: median	NA	NA
95% CrILB	NA	NA
95% CrIUB	NA	NA
ESS	NA	NA
Expected results for Posterior: mean	NA	NA
Expected results for Posterior: SD	NA	NA
Expected results for Posterior: median	NA	NA
95% CrILB	NA	NA
95% CrIUB	NA	NA
ESS	NA	NA

6.1.5   Scenario 5 - Heterogeneous Data(Medium)

Scenario 5 describes a binary endpoint for a medium heterogenous scenario between the historical data, moderate noise at a 5% tau, moderate censoring at 5%, all events observed at a 90%power and no planned prior data conflict.

```
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0.05, time = 12),
  SimStudy_accr = 1,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 93,
  SimStudy_censor_type = 2,
  nStudy = 6,
  tau = 0.05,
  prior_data_conflict = FALSE,
  pdc_hz = NA,
  SAF_TOPIC = "Scen5",
  seed = 1701628373
)
```

```
##        STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE  TOT_EXP DOSE FREQ LENGTH TREAT
## 1_g1 Study#1    1  g1 200     Scen5        24 336.2761  999  999    999 Scen5
## 2_g1 Study#2    1  g1 200     Scen5        35 328.5856  999  999    999 Scen5
## 3_g1 Study#3    1  g1 200     Scen5        26 319.0432  999  999    999 Scen5
## 4_g1 Study#4    1  g1 200     Scen5        36 319.4839  999  999    999 Scen5
## 5_g1 Study#5    1  g1 200     Scen5        39 282.5063  999  999    999 Scen5
## 6_g1 Study#6    0  g1 200     Scen5        25 289.3660  999  999    999 Scen5
## 1_g2 Study#1    1  g2 200     Scen5        68 295.3881  999  999    999 Scen5
## 2_g2 Study#2    1  g2 200     Scen5        55 310.0651  999  999    999 Scen5
## 3_g2 Study#3    1  g2 200     Scen5        63 290.2667  999  999    999 Scen5
## 4_g2 Study#4    1  g2 200     Scen5        54 288.7203  999  999    999 Scen5
## 5_g2 Study#5    1  g2 200     Scen5        52 283.8704  999  999    999 Scen5
## 6_g2 Study#6    0  g2 200     Scen5        66 263.6880  999  999    999 Scen5
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                         csv group          analysis saf_topic       seed
## Heterogenous Data  Scen05.csv   g1 Incidence proportion    Scen05 1701628373
##                        pool    tau heterog  ESS rob_weight nta_event nta_npat
## Heterogenous Data      TRUE HalfNormal   Large elir        0.4        25       200
```

Characteristic	Lower Threshold	Upper Threshold
Expected MAP Prior: mean	0.161702249968323	0.166223676863546
Expected MAP Prior: SD	0.0384235793012453	0.0533049133575082
Expected MAP Prior: median	0.157629581894639	0.161583610380999
95% CrILB	0.0804921953220503	0.0965171835619208
95% CrIUB	0.249973511572156	0.29506461207034
ESS	114.61196054288	178.708376849547
Expected robustified MAP Prior: mean	0.297034484315248	0.299855152066132
Expected robustified MAP Prior: SD	0.247451070010251	0.248676467221644
Expected robustified MAP Prior: median	0.174164037364888	0.17876349761284
95% CrILB	0.0516018491604339	0.0590468499234017
95% CrIUB	0.937469490398029	0.937540242270999
ESS	58.8516205513915	94.1381660186474
Expected results for Likelihood: mean	0.125	0.125
Expected results for Likelihood: SD	0.0233271135988943	0.0233271135988943
Expected results for Likelihood: median	0.123749460636806	0.123749460636806
95% CrILB	0.0829759759727852	0.0829759759727852
95% CrIUB	0.17411612240213	0.17411612240213
ESS	NA	NA
Expected results for Posterior: mean	0.138966376990468	0.141331919643552
Expected results for Posterior: SD	0.0188279019215256	0.0206031218898134
Expected results for Posterior: median	0.139454853537392	0.142819399788163
95% CrILB	0.0978159237699362	0.102490491086824
95% CrIUB	0.176747080922505	0.179046287562127
ESS	NA	NA

6.1.6   Scenario 6 - High Dropout

Scenario 6 describes a binary endpoint scenario with huge dropout within the current trial, some noise at a 2% tau, some event being observed at a 90% power, homogeneous data and no planned prior data conflict.

```
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0.3, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 95,
  SimStudy_censor_type = 2,
  nStudy = 6,
  tau = 0.02,
  prior_data_conflict = FALSE,
  pdc_hz = NA,
  SAF_TOPIC = "Scen6",
  seed = 1701628373
)
```

```
##        STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE  TOT_EXP DOSE FREQ LENGTH TREAT
## 1_g1 Study#1    1  g1 200     Scen6        26 291.6589  999  999    999 Scen6
## 2_g1 Study#2    1  g1 200     Scen6        27 225.3005  999  999    999 Scen6
## 3_g1 Study#3    1  g1 200     Scen6        28 292.3146  999  999    999 Scen6
## 4_g1 Study#4    1  g1 200     Scen6        28 268.4692  999  999    999 Scen6
## 5_g1 Study#5    1  g1 200     Scen6        40 212.6690  999  999    999 Scen6
## 6_g1 Study#6    0  g1 200     Scen6        24 198.0645  999  999    999 Scen6
## 1_g2 Study#1    1  g2 200     Scen6        56 226.4060  999  999    999 Scen6
## 2_g2 Study#2    1  g2 200     Scen6        52 203.6631  999  999    999 Scen6
## 3_g2 Study#3    1  g2 200     Scen6        55 255.6490  999  999    999 Scen6
## 4_g2 Study#4    1  g2 200     Scen6        47 221.9167  999  999    999 Scen6
## 5_g2 Study#5    1  g2 200     Scen6        45 238.6339  999  999    999 Scen6
## 6_g2 Study#6    0  g2 200     Scen6        54 219.5831  999  999    999 Scen6
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                   csv group            analysis saf_topic       seed pool
## High Dropout Scen06.csv    g1 Incidence proportion    Scen06 1701628373 TRUE
##                   tau  heterog  ESS rob_weight nta_event nta_npat
## High Dropout HalfNormal Moderate elir      0.14        31      200
```

Characteristic	Lower Threshold	Upper Threshold
Expected MAP Prior: mean	0.148748955474947	0.150744738445545
Expected MAP Prior: SD	0.0185868339720032	0.0271307753694242
Expected MAP Prior: median	0.148084908078525	0.150014412602078
95% CrILB	0.100823105787152	0.115828638363774
95% CrIUB	0.187366111442526	0.211422878502643
ESS	250.003883014752	449.599905639595

Characteristic	Lower Threshold	Upper Threshold
Expected robustified MAP Prior: mean	0.19792413618616	0.19964305115916
Expected robustified MAP Prior: SD	0.163350821659274	0.164409241935166
Expected robustified MAP Prior: median	0.150553105048393	0.152345830142052
95% CrILB	0.0915713033122365	0.108753785149937
95% CrIUB	0.82142857142857	0.821453597194165
ESS	205.878681242996	372.161627396065
Expected results for Likelihood: mean	0.155	0.155
Expected results for Likelihood: SD	0.0255267881924633	0.0255267881924633
Expected results for Likelihood: median	0.153848972465443	0.153848972465443
95% CrILB	0.108364536862043	0.108364536862043
95% CrIUB	0.208163854001394	0.208163854001394
ESS	NA	NA
Expected results for Posterior: mean	0.150653911759225	0.151868960362497
Expected results for Posterior: SD	0.0140554389948649	0.0162325012399689
Expected results for Posterior: median	0.150095008213379	0.151546216697458
95% CrILB	0.121057885359172	0.125555313743539
95% CrIUB	0.179808487104747	0.185238480000413
ESS	NA	NA

6.1.7 Scenario 7 - High Heterogeneity

Scenario 7 describes a binary endpoint scenario with high heterogeneity between historical data, moderate censoring in current trial, moderate noise at a 2% tau, all events observed at a 90% power, with no planned prior data conflict.

```
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0.05, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 93,
  SimStudy_censor_type = 2,
  nStudy = 6,
  tau = 0.15,
  prior_data_conflict = FALSE,
  pdc_hz = NA,
  SAF_TOPIC = "Scen7",
  seed = 1701416989
)
```

```
##       STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE   TOT_EXP DOSE FREQ LENGTH TREAT
## 1_g1 Study#1    1  g1 200     Scen7        32 222.47360  999  999    999 Scen7
## 2_g1 Study#2    1  g1 200     Scen7        27 270.34094  999  999    999 Scen7
## 3_g1 Study#3    1  g1 200     Scen7        32 271.08747  999  999    999 Scen7
## 4_g1 Study#4    1  g1 200     Scen7        36 116.93497  999  999    999 Scen7
## 5_g1 Study#5    1  g1 200     Scen7        29 111.37228  999  999    999 Scen7
```

```
## 6_g1 Study#6   0  g1 200    Scen7    23 163.68689 999 999   999 Scen7
## 1_g2 Study#1   1  g2 200    Scen7    59 189.49417 999 999   999 Scen7
## 2_g2 Study#2   1  g2 200    Scen7    62 284.62991 999 999   999 Scen7
## 3_g2 Study#3   1  g2 200    Scen7    58 210.80011 999 999   999 Scen7
## 4_g2 Study#4   1  g2 200    Scen7    56  77.53109 999 999   999 Scen7
## 5_g2 Study#5   1  g2 200    Scen7    62 118.22857 999 999   999 Scen7
## 6_g2 Study#6   0  g2 200    Scen7    68  97.68813 999 999   999 Scen7
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                      csv group        analysis saf_topic      seed
## High Heterogeneity Scen07.csv   g1 Incidence proportion    Scen07 1701416989
##                   pool     tau    heterog  ESS rob_weight nta_event
## High Heterogeneity TRUE HalfNormal Very Large elir        0.2        35
##                   nta_npat
## High Heterogeneity    200
```

Characteristic	Lower Threshold	Upper Threshold
Expected MAP Prior: mean	0.156752405844846	0.16089753006357
Expected MAP Prior: SD	0.0292449392789426	0.0501663750979713
Expected MAP Prior: median	0.15491860116048	0.15715431955336
95% CrILB	0.0857312078143469	0.108828994903086
95% CrIUB	0.218133253083768	0.243188809686601
ESS	245.087287695845	316.300688739912
Expected robustified MAP Prior: mean	0.225437060048366	0.228810922242153
Expected robustified MAP Prior: SD	0.189677711234007	0.192574846625508
Expected robustified MAP Prior: median	0.159264510355454	0.161612263400314
95% CrILB	0.0642282916886863	0.0886840406176512
95% CrIUB	0.874969548471955	0.877137991297914
ESS	185.14275667454	241.213566982589
Expected results for Likelihood: mean	0.175	0.175
Expected results for Likelihood: SD	0.0268008130863516	0.0268008130863516
Expected results for Likelihood: median	0.173915464398537	0.173915464398537
95% CrILB	0.125669597585709	0.125669597585709
95% CrIUB	0.230481950063388	0.230481950063388
ESS	NA	NA
Expected results for Posterior: mean	0.163093124613875	0.164783506331725
Expected results for Posterior: SD	0.0163607868222977	0.0178808262731581
Expected results for Posterior: median	0.161774891820203	0.163978463428382
95% CrILB	0.132749634468039	0.134721436879043
95% CrIUB	0.198137748882925	0.205091421556515
ESS	NA	NA

6.1.8 Scenario 8 - Bad Scenario

Scenario 8 describes a binary endpoint for a bad scenario with huge censoring in the current trial, huge noise, little events observed in the current trial, heterogeneous historical data and no planned prior data conflict.

```
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0.3, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 93,
  SimStudy_censor_type = 2,
  nStudy = 6,
  tau = 0.15,
  prior_data_conflict = FALSE,
  pdc_hz = NA,
  SAF_TOPIC = "Scen8",
  seed = 1701652217
)
```

```
##          STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE  TOT_EXP DOSE FREQ LENGTH TREAT
## 1_g1 Study#1    1  g1 200     Scen8        22 297.7669  999  999    999 Scen8
## 2_g1 Study#2    1  g1 200     Scen8        31 298.1832  999  999    999 Scen8
## 3_g1 Study#3    1  g1 200     Scen8        21 307.9312  999  999    999 Scen8
## 4_g1 Study#4    1  g1 200     Scen8        21 379.2739  999  999    999 Scen8
## 5_g1 Study#5    1  g1 200     Scen8        28 405.2051  999  999    999 Scen8
## 6_g1 Study#6    0  g1 200     Scen8        30 368.8481  999  999    999 Scen8
## 1_g2 Study#1    1  g2 200     Scen8        53 234.0924  999  999    999 Scen8
## 2_g2 Study#2    1  g2 200     Scen8        45 226.9392  999  999    999 Scen8
## 3_g2 Study#3    1  g2 200     Scen8        55 211.8717  999  999    999 Scen8
## 4_g2 Study#4    1  g2 200     Scen8        56 348.7668  999  999    999 Scen8
## 5_g2 Study#5    1  g2 200     Scen8        46 375.9676  999  999    999 Scen8
## 6_g2 Study#6    0  g2 200     Scen8        45 284.3348  999  999    999 Scen8
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                  csv group        analysis saf_topic      seed pool
## Bad Scenario Scen08.csv   g1 Incidence proportion   Scen08 1701652217 TRUE
##                 tau heterog  ESS rob_weight nta_event nta_npat
## Bad Scenario HalfNormal  Large elir      0.2         25      200
```

Characteristic	Lower Threshold	Upper Threshold
Expected MAP Prior: mean	0.124149578724249	0.127475281325506
Expected MAP Prior: SD	0.0277928230445493	0.0390384757915474
Expected MAP Prior: median	0.121907160550387	0.124275701839677
95% CrILB	0.0673460578121984	0.0784488478524441
95% CrIUB	0.184158397736284	0.211139328836811
ESS	198.658314463714	263.72905362793

Characteristic	Lower Threshold	Upper Threshold
Expected robustified MAP Prior: mean	0.199320297345458	0.202022684776386
Expected robustified MAP Prior: SD	0.199102888651521	0.200381648773237
Expected robustified MAP Prior: median	0.126701788969984	0.129228844424758
95% CrILB	0.0583059114145427	0.0698120997921859
95% CrIUB	0.874983493747324	0.875074048981225
ESS	150.581920865789	201.204234587357
Expected results for Likelihood: mean	0.125	0.125
Expected results for Likelihood: SD	0.0233271135988943	0.0233271135988943
Expected results for Likelihood: median	0.123749460636806	0.123749460636806
95% CrILB	0.0829759759727852	0.0829759759727852
95% CrIUB	0.17411612240213	0.17411612240213
ESS	NA	NA
Expected results for Posterior: mean	0.123556219260721	0.125095399662725
Expected results for Posterior: SD	0.0146163434901418	0.0157901337836749
Expected results for Posterior: median	0.122977132202056	0.124680563493779
95% CrILB	0.0946528697249493	0.0973049989541528
95% CrIUB	0.154077626792942	0.157973423067448
ESS	NA	NA

6.1.9 Scenario 9 - Good Scenario

Scenario 9 describes a binary endpoint for a good scenario with low censoring in the current trial,small noise, majority of the events being observed and homogeneous historical data.

```
SimTestData(
  SimStudy_nPat = c(g1 = 300, g2 = 300),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 24,
  SimStudy_NObsEvt = 0.999,
  SimStudy_censor_type = 1,
  nStudy = 8,
  tau = 0.01,
  prior_data_conflict = FALSE,
  pdc_hz = NA,
  SAF_TOPIC = "Scen9",
  seed = 1701655293
)
```

```
##       STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE  TOT_EXP DOSE FREQ LENGTH TREAT
## 1_g1 Study#1    1  g1 300     Scen9       260 2838.989  999  999    999 Scen9
## 2_g1 Study#2    1  g1 300     Scen9       259 2624.533  999  999    999 Scen9
## 3_g1 Study#3    1  g1 300     Scen9       251 2933.272  999  999    999 Scen9
## 4_g1 Study#4    1  g1 300     Scen9       251 2984.729  999  999    999 Scen9
## 5_g1 Study#5    1  g1 300     Scen9       259 2667.259  999  999    999 Scen9
## 6_g1 Study#6    1  g1 300     Scen9       265 2774.955  999  999    999 Scen9
```

```
## 7_g1 Study#7    1  g1 300      Scen9      255 2665.750  999  999    999 Scen9
## 8_g1 Study#8    0  g1 300      Scen9      261 2691.265  999  999    999 Scen9
## 1_g2 Study#1    1  g2 300      Scen9      292 1550.852  999  999    999 Scen9
## 2_g2 Study#2    1  g2 300      Scen9      295 1646.227  999  999    999 Scen9
## 3_g2 Study#3    1  g2 300      Scen9      297 1360.433  999  999    999 Scen9
## 4_g2 Study#4    1  g2 300      Scen9      289 1676.768  999  999    999 Scen9
## 5_g2 Study#5    1  g2 300      Scen9      294 1678.219  999  999    999 Scen9
## 6_g2 Study#6    1  g2 300      Scen9      295 1628.496  999  999    999 Scen9
## 7_g2 Study#7    1  g2 300      Scen9      295 1628.708  999  999    999 Scen9
## 8_g2 Study#8    0  g2 300      Scen9      295 1486.654  999  999    999 Scen9
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"


##                    csv group           analysis saf_topic      seed pool
## Good Scenario Scen09.csv   g1 Incidence proportion    Scen09 1701655293 TRUE
##                    tau heterog  ESS rob_weight nta_event nta_npat
## Good Scenario HalfNormal   Small elir      0.05        175       200
```

Characteristic	Lower Threshold	Upper Threshold
Expected MAP Prior: mean	0.856316722151938	0.857450167520614
Expected MAP Prior: SD	0.00998643549140604	0.0138988599144546
Expected MAP Prior: median	0.856554974465311	0.857628176257154
95% CrILB	0.82661630490516	0.837250066966443
95% CrIUB	0.875316583937026	0.883110106052011
ESS	852.150682059392	1325.05068865646
Expected robustified MAP Prior: mean	0.838500822325505	0.839577616974383
Expected robustified MAP Prior: SD	0.101493341158459	0.101936748781012
Expected robustified MAP Prior: median	0.85610424528955	0.857108924256142
95% CrILB	0.499999999885896	0.5
95% CrIUB	0.876766162726735	0.885518382702662
ESS	801.012506262468	1244.31477040346
Expected results for Likelihood: mean	0.875	0.875
Expected results for Likelihood: SD	0.0233271135988934	0.0233271135988934
Expected results for Likelihood: median	0.876250539363194	0.876250539363194
95% CrILB	0.82588387759787	0.82588387759787
95% CrIUB	0.917024024027215	0.917024024027215
ESS	NA	NA
Expected results for Posterior: mean	0.859114863859739	0.860387967331582
Expected results for Posterior: SD	0.00918175307849913	0.0111737741917695
Expected results for Posterior: median	0.858971512541915	0.860105196096467
95% CrILB	0.839424523145348	0.841778967264418
95% CrIUB	0.877121593766657	0.883830187428603
ESS	NA	NA

6.1.10 Scenario 10 - Favoured Control

Scenario 10 describes a binary endpoint for a favored control scenario with no censoring in the current trial, no noise, all events being observed, homogeneous historical data, heavy prior data conflict and the hazard ratio in favor of the control group.

```
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.2, g2 = 0.1),
  SimStudy_dropout = c(rate = 0.05, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 93,
  SimStudy_censor_type = 2,
  nStudy = 6,
  tau = 0.02,
  prior_data_conflict = TRUE,
  pdc_hz = 1.2,
  SAF_TOPIC = "Scen10",
  seed = 1701673095
)
```

```
## Warning in rexp(nPat[i], hz[i]): NAs produced
```

```
##         STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE     TOT_EXP DOSE FREQ LENGTH
## 1_g1 Study#1    1  g1 200    Scen10        54 234.482445  999  999    999
## 2_g1 Study#2    1  g1 200    Scen10        42 200.954605  999  999    999
## 3_g1 Study#3    1  g1 200    Scen10        59 233.239862  999  999    999
## 4_g1 Study#4    1  g1 200    Scen10        51 204.363002  999  999    999
## 5_g1 Study#5    1  g1 200    Scen10        52 170.728016  999  999    999
## 6_g1 Study#6    0  g1 200    Scen10        93  -6.482995  999  999    999
## 1_g2 Study#1    1  g2 200    Scen10        36 282.421760  999  999    999
## 2_g2 Study#2    1  g2 200    Scen10        46 214.300246  999  999    999
## 3_g2 Study#3    1  g2 200    Scen10        32 318.335395  999  999    999
## 4_g2 Study#4    1  g2 200    Scen10        37 243.939964  999  999    999
## 5_g2 Study#5    1  g2 200    Scen10        39 244.166712  999  999    999
## 6_g2 Study#6    0  g2 200    Scen10        NA         NA  999  999    999
##         TREAT
## 1_g1 Scen10
## 2_g1 Scen10
## 3_g1 Scen10
## 4_g1 Scen10
## 5_g1 Scen10
## 6_g1 Scen10
## 1_g2 Scen10
## 2_g2 Scen10
## 3_g2 Scen10
## 4_g2 Scen10
## 5_g2 Scen10
## 6_g2 Scen10
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                        csv group          analysis saf_topic      seed pool
## Favored Control Scen10.csv   g1 Incidence proportion    Scen10 1701673095 TRUE
##                    tau heterog  ESS rob_weight nta_event nta_npat
## Favored Control HalfNormal  Small elir      0.6       175      200
```

Characteristic	Lower Threshold	Upper Threshold
Expected MAP Prior: mean	0.257483739385017	0.259437314351065
Expected MAP Prior: SD	0.0178126332526662	0.0251663324182848
Expected MAP Prior: median	0.256986735748943	0.259105162498246
95% CrILB	0.210797565657957	0.225177168293556
95% CrIUB	0.293257651366777	0.313091829785504
ESS	379.209812410461	643.391695463927
Expected robustified MAP Prior: mean	0.402993377770819	0.403774917973046
Expected robustified MAP Prior: SD	0.2530230311029	0.253487298070021
Expected robustified MAP Prior: median	0.274154254371167	0.27912018353434
95% CrILB	0.0416605330036899	0.0416666666662217
95% CrIUB	0.958333333333333	0.958334443917622
ESS	116.753983604762	201.721530304303
Expected results for Likelihood: mean	0.875	0.875
Expected results for Likelihood: SD	0.0233271135988934	0.0233271135988934
Expected results for Likelihood: median	0.876250539363194	0.876250539363194
95% CrILB	0.82588387759787	0.82588387759787
95% CrIUB	0.917024024027215	0.917024024027215
ESS	NA	NA
Expected results for Posterior: mean	0.871287128710477	0.871287128712871
Expected results for Posterior: SD	0.0235040996373885	0.0235040996410732
Expected results for Posterior: median	0.872507529148914	0.872509900792152
95% CrILB	0.821859247701957	0.821914576408324
95% CrIUB	0.91371988078872	0.913732054083703
ESS	NA	NA

6.1.11 Scenario 11 - Continued study duration with Realistic Setting

Scenario 11 describes a binary endpoint for a realistic situation where the study continued regardless of when the proposed number of events has been observed. Characteristics of this scenario includes a drop out rate of 5%, noise at a 5% tau, homogeneous historical data and no planned prior data conflict planned.

```
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0.05, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 24,
  SimStudy_NObsEvt = 93,
  SimStudy_censor_type = 1,
  nStudy = 6,
  tau = 0.02,
  prior_data_conflict = FALSE,
```

```
  pdc_hz = NA,
  SAF_TOPIC = "Scen11",
  seed = 1701876972
)
```

```
##        STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE   TOT_EXP DOSE FREQ LENGTH   TREAT
## 1_g1 Study#1    1  g1 200    Scen11       170 1871.1930  999  999    999 Scen11
## 2_g1 Study#2    1  g1 200    Scen11       173 1630.1105  999  999    999 Scen11
## 3_g1 Study#3    1  g1 200    Scen11       168 1744.6636  999  999    999 Scen11
## 4_g1 Study#4    1  g1 200    Scen11       170 1904.9560  999  999    999 Scen11
## 5_g1 Study#5    1  g1 200    Scen11       166 1748.6775  999  999    999 Scen11
## 6_g1 Study#6    0  g1 200    Scen11       162 1879.6921  999  999    999 Scen11
## 1_g2 Study#1    1  g2 200    Scen11       191  910.6017  999  999    999 Scen11
## 2_g2 Study#2    1  g2 200    Scen11       192  957.8531  999  999    999 Scen11
## 3_g2 Study#3    1  g2 200    Scen11       196  922.9765  999  999    999 Scen11
## 4_g2 Study#4    1  g2 200    Scen11       198  927.3806  999  999    999 Scen11
## 5_g2 Study#5    1  g2 200    Scen11       193 1027.3669  999  999    999 Scen11
## 6_g2 Study#6    0  g2 200    Scen11       196 1068.8192  999  999    999 Scen11
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                                                        csv group
## Continued Study Duration with Realistic Setting Scen11.csv    g1
##                                                   analysis saf_topic
## Continued Study Duration with Realistic Setting Incidence proportion    Scen11
##                                                        seed pool        tau
## Continued Study Duration with Realistic Setting 1701876972 TRUE HalfNormal
##                                                     heterog  ESS rob_weight
## Continued Study Duration with Realistic Setting    Small elir      0.05
##                                                   nta_event nta_npat
## Continued Study Duration with Realistic Setting       170      200
```

Characteristic	Lower Threshold	Upper Threshold
Expected MAP Prior: mean	0.845825131903068	0.847181313098101
Expected MAP Prior: SD	0.0133308466629699	0.0173455562974319
Expected MAP Prior: median	0.846099745674875	0.847625662083459
95% CrILB	0.807659841713298	0.820068835845819
95% CrIUB	0.870716818678199	0.880081747554867
ESS	503.332249765084	761.551232558511
Expected robustified MAP Prior: mean	0.828533386247795	0.8298223366671
Expected robustified MAP Prior: SD	0.100117650172509	0.100687660980764
Expected robustified MAP Prior: median	0.845389693982147	0.846968669317222
95% CrILB	0.499999999999923	0.5
95% CrIUB	0.872530843067065	0.881256731939332
ESS	470.446311800306	708.080942674032
Expected results for Likelihood: mean	0.85	0.85
Expected results for Likelihood: SD	0.0251858761652038	0.0251858761652038
Expected results for Likelihood: median	0.851167634875943	0.851167634875943
95% CrILB	0.797459935170381	0.797459935170381

Characteristic	Lower Threshold	Upper Threshold
95% CrIUB	0.895917570916335	0.895917570916335
ESS	NA	NA
Expected results for Posterior: mean	0.846821214192104	0.847831039476398
Expected results for Posterior: SD	0.011715527826912	0.0133606275698494
Expected results for Posterior: median	0.84679518002293	0.848106200044125
95% CrILB	0.820205095637786	0.82398962994517
95% CrIUB	0.869003474803494	0.873106219194571
ESS	NA	NA

6.1.12 Scenario 12 - Continued study duration with Worst Setting

Scenario 12 describes a binary endpoint for a scenario with a worst case scenario (scenario 4) that continued till the end of the proposed study duration. The scenario characteristics includes huge censoring, huge noise, little events observed, heterogeneous historical and huge prior data conflict.

```
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0.05, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = NA,
  SimStudy_NObsEvt = 400,
  SimStudy_censor_type = 2,
  nStudy = 6,
  tau = 0.15,
  prior_data_conflict = TRUE,
  pdc_hz = c(g1 = 0.05, g2 = 0.1),
  SAF_TOPIC = "Scen12",
  seed = 1701878308
)
```

```
##        STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE   TOT_EXP DOSE FREQ LENGTH  TREAT
## 1_g1 Study#1    1  g1 200    Scen12       193 2145.2002  999  999    999 Scen12
## 2_g1 Study#2    1  g1 200    Scen12       189 2026.7007  999  999    999 Scen12
## 3_g1 Study#3    1  g1 200    Scen12       192 2099.1503  999  999    999 Scen12
## 4_g1 Study#4    1  g1 200    Scen12       193 2200.2265  999  999    999 Scen12
## 5_g1 Study#5    1  g1 200    Scen12       189 2060.4879  999  999    999 Scen12
## 6_g1 Study#6    0  g1 200    Scen12       193 3214.6233  999  999    999 Scen12
## 1_g2 Study#1    1  g2 200    Scen12       196  927.0819  999  999    999 Scen12
## 2_g2 Study#2    1  g2 200    Scen12       193 1097.0120  999  999    999 Scen12
## 3_g2 Study#3    1  g2 200    Scen12       196 1112.5535  999  999    999 Scen12
## 4_g2 Study#4    1  g2 200    Scen12       195 1489.9002  999  999    999 Scen12
## 5_g2 Study#5    1  g2 200    Scen12       198 1575.7302  999  999    999 Scen12
## 6_g2 Study#6    0  g2 200    Scen12       191 1811.5262  999  999    999 Scen12
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                                                csv group
## Continued Study Duration with Worst Setting Scen12.csv    g1
##                                                   analysis saf_topic
## Continued Study Duration with Worst Setting Incidence proportion    Scen12
##                                                 seed pool      tau heterog
## Continued Study Duration with Worst Setting 1701878308 TRUE HalfNormal   Large
##                                                ESS rob_weight nta_event nta_npat
## Continued Study Duration with Worst Setting elir        0.5        30      200
```

Characteristic	Lower Threshold	Upper Threshold
Expected MAP Prior: mean	NA	NA
Expected MAP Prior: SD	NA	NA
Expected MAP Prior: median	NA	NA
95% CrILB	NA	NA
95% CrIUB	NA	NA
ESS	NA	NA
Expected robustified MAP Prior: mean	NA	NA
Expected robustified MAP Prior: SD	NA	NA
Expected robustified MAP Prior: median	NA	NA
95% CrILB	NA	NA
95% CrIUB	NA	NA
ESS	NA	NA
Expected results for Likelihood: mean	NA	NA
Expected results for Likelihood: SD	NA	NA
Expected results for Likelihood: median	NA	NA
95% CrILB	NA	NA
95% CrIUB	NA	NA
ESS	NA	NA
Expected results for Posterior: mean	NA	NA
Expected results for Posterior: SD	NA	NA
Expected results for Posterior: median	NA	NA
95% CrILB	NA	NA
95% CrIUB	NA	NA
ESS	NA	NA

6.1.13 Scenario 13 - High Dropout & too few people observed

Scenario 13 describes a binary endpoint for a situation with high dropout rate 0f 30%, small noise at a 2% tau, homogeneous historical data, few events being observed and no planned prior data conflict.

```
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0.3, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
```

```
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 50,
  SimStudy_censor_type = 2,
  nStudy = 6,
  tau = 0.02,
  prior_data_conflict = FALSE,
  pdc_hz = NA,
  SAF_TOPIC = "Scen13",
  seed = 1701879909
)
```

```
##         STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE     TOT_EXP DOSE FREQ LENGTH
## 1_g1 Study#1    1  g1 200    Scen13        11  13.585224  999  999    999
## 2_g1 Study#2    1  g1 200    Scen13        17  58.318673  999  999    999
## 3_g1 Study#3    1  g1 200    Scen13        16  31.614870  999  999    999
## 4_g1 Study#4    1  g1 200    Scen13        15  37.790334  999  999    999
## 5_g1 Study#5    1  g1 200    Scen13        12   2.984491  999  999    999
## 6_g1 Study#6    0  g1 200    Scen13        11 -49.492541  999  999    999
## 1_g2 Study#1    1  g2 200    Scen13        28   3.305205  999  999    999
## 2_g2 Study#2    1  g2 200    Scen13        21  44.281966  999  999    999
## 3_g2 Study#3    1  g2 200    Scen13        27  -9.716870  999  999    999
## 4_g2 Study#4    1  g2 200    Scen13        25   8.577101  999  999    999
## 5_g2 Study#5    1  g2 200    Scen13        30 -29.258983  999  999    999
## 6_g2 Study#6    0  g2 200    Scen13        33 -26.851666  999  999    999
##         TREAT
## 1_g1 Scen13
## 2_g1 Scen13
## 3_g1 Scen13
## 4_g1 Scen13
## 5_g1 Scen13
## 6_g1 Scen13
## 1_g2 Scen13
## 2_g2 Scen13
## 3_g2 Scen13
## 4_g2 Scen13
## 5_g2 Scen13
## 6_g2 Scen13
```

The characteristics and thresholds for the simulation is as in the table below:

6.2 Time To Event Endpoint

6.2.1 Scenario 1 - Best Case Scenario

```
# Scen1
SimTestData(
  SimStudy_nPat = c(g1 = 300, g2 = 300),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0, time = 12),
  SimStudy_accr = 1,
  SimStudy_accr_method = "Uniform",
```

```
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 0.999,
  SimStudy_censor_type = 2,
  nStudy = 10,
  tau = 0,
  prior_data_conflict = FALSE,
  pdc_hz = NA,
  SAF_TOPIC = "Scen1",
  seed = 1699874539
)
```

```
##          STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE  TOT_EXP DOSE FREQ LENGTH TREAT
## 1_g1    Study#1     1  g1 300     Scen1       299 2828.715  999  999    999 Scen1
## 2_g1    Study#2     1  g1 300     Scen1       299 2882.367  999  999    999 Scen1
## 3_g1    Study#3     1  g1 300     Scen1       299 3236.408  999  999    999 Scen1
## 4_g1    Study#4     1  g1 300     Scen1       299 3085.252  999  999    999 Scen1
## 5_g1    Study#5     1  g1 300     Scen1       299 2984.353  999  999    999 Scen1
## 6_g1    Study#6     1  g1 300     Scen1       299 3305.953  999  999    999 Scen1
## 7_g1    Study#7     1  g1 300     Scen1       299 2975.530  999  999    999 Scen1
## 8_g1    Study#8     1  g1 300     Scen1       299 3103.969  999  999    999 Scen1
## 9_g1    Study#9     1  g1 300     Scen1       299 2763.876  999  999    999 Scen1
## 10_g1 Study#10     0  g1 300     Scen1       299 3044.691  999  999    999 Scen1
## 1_g2    Study#1     1  g2 300     Scen1       300 1466.836  999  999    999 Scen1
## 2_g2    Study#2     1  g2 300     Scen1       300 1604.556  999  999    999 Scen1
## 3_g2    Study#3     1  g2 300     Scen1       300 1428.295  999  999    999 Scen1
## 4_g2    Study#4     1  g2 300     Scen1       300 1472.222  999  999    999 Scen1
## 5_g2    Study#5     1  g2 300     Scen1       300 1678.517  999  999    999 Scen1
## 6_g2    Study#6     1  g2 300     Scen1       300 1504.812  999  999    999 Scen1
## 7_g2    Study#7     1  g2 300     Scen1       300 1626.479  999  999    999 Scen1
## 8_g2    Study#8     1  g2 300     Scen1       300 1480.283  999  999    999 Scen1
## 9_g2    Study#9     1  g2 300     Scen1       300 1644.251  999  999    999 Scen1
## 10_g2 Study#10     0  g2 300     Scen1       300 1519.465  999  999    999 Scen1
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                            csv group          analysis saf_topic        seed
## Best case scenario scen01.csv    g1 Incidence proportion    Scen01 1699874539
##                      pool       tau heterog  ESS rob_weight nta_event nta_npat
## Best case scenario  TRUE HalfNormal   Small elir       0.05       194      200
```

Characteristic	Lower Threshold	Upper Threshold
log Expected MAP Prior: mean	-2.31295176298674	-2.30819013799256
log Expected MAP Prior: SD	0.0391107636048691	0.0443209150381256
log Expected MAP Prior: median	-2.31307113720592	-2.30866615071351
log 95% CrILB	-2.40665682037742	-2.3868178634415
log 95% CrIUB	-2.23437029770634	-2.21277529920943

Characteristic	Lower Threshold	Upper Threshold
log ESS	733.394166832418	4702431.19835056
log Expected robustified MAP Prior: mean	-2.1923041748374	-2.18778063109293
log Expected robustified MAP Prior: SD	0.571962576548747	0.57297860244359
log Expected robustified MAP Prior: median	-2.31086645324604	-2.30673431285901
log 95% CrILB	-2.40891749957024	-2.3877021008846
log 95% CrIUB	0.0999778971663519	0.100025336781002
log ESS	695.92719757707	4464851.05575332
log Expected results for Likelihood: mean	-2.30258509299405	-2.30258509299405
log Expected results for Likelihood: SD	0.0999999999999989	0.0999999999999989
log Expected results for Likelihood: median	-2.30258509299405	-2.30258509299405
log 95% CrILB	-2.49858149144805	-2.49858149144805
log 95% CrIUB	-2.10658869454004	-2.10658869454004
log ESS	NA	NA
log Expected results for Posterior: mean	-2.31155179995562	-2.30790391751987
log Expected results for Posterior: SD	0.0339559431665446	0.0368272757087718
log Expected results for Posterior: median	-2.31195149811814	-2.30838094760477
log 95% CrILB	-2.3872376902736	-2.37598711468948
log 95% CrIUB	-2.24106971406972	-2.22853576292699
log ESS	NA	NA
exp Expected MAP Prior: mean	0.0990521157134907	0.0995307677358296
exp Expected MAP Prior: SD	0.00389161376220243	0.004440592476031
exp Expected MAP Prior: median	0.0989568742684962	0.0993937394504599
exp 95% CrILB	0.0901160658225069	0.0919217267262796
exp 95% CrIUB	0.107059524807587	0.109396618483642
exp ESS	NA	NA
exp Expected robustified MAP Prior: mean	0.0990521157134907	0.0995307677358296
exp Expected robustified MAP Prior: SD	0.00389161376220243	0.004440592476031
exp Expected robustified MAP Prior: median	0.0989568742684962	0.0993937394504599
exp 95% CrILB	0.0901160658225069	0.0919217267262796
exp 95% CrIUB	0.107059524807587	0.109396618483642
exp ESS	NA	NA
exp Expected results for Likelihood: mean	NA	NA
exp Expected results for Likelihood: SD	NA	NA
exp Expected results for Likelihood: median	NA	NA
exp 95% CrILB	NA	NA
exp 95% CrIUB	NA	NA
exp ESS	NA	NA
exp Expected results for Posterior: mean	0.0991429475421018	0.0995273670928804
exp Expected results for Posterior: SD	0.00335704364550322	0.00369156536061414
exp Expected results for Posterior: median	0.0990538740485409	0.0994353366119162
exp 95% CrILB	0.0918635264067453	0.0928807471406947
exp 95% CrIUB	0.106302765206118	0.107757035365127
exp ESS	NA	NA

6.2.2 Scenario 2 - Strong Prior Data Conflict

Scenario 2 describes a test case scenario for a binary endpoint with a strong prior data conflict between the historical and current trials. The characteristics of this scenario includes no censoring in the current trial, no noise, all events being observed, homogeneous historical data and heavy prior data conflict.

```
# Scen2
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.3),
  SimStudy_dropout = c(rate = 0, time = 12),
  SimStudy_accr = 1,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 0.9,
  SimStudy_censor_type = 2,
  nStudy = 10,
  tau = 0.01,
  prior_data_conflict = TRUE,
  pdc_hz = c(g1 = 0.4, g2 = 0.05),
  SAF_TOPIC = "Scen2",
  seed = 1701611344
)
```

```
##          STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE   TOT_EXP DOSE FREQ LENGTH
## 1_g1    Study#1    1  g1 200     Scen2       161 1530.2128  999  999    999
## 2_g1    Study#2    1  g1 200     Scen2       162 1528.7454  999  999    999
## 3_g1    Study#3    1  g1 200     Scen2       160 1660.3443  999  999    999
## 4_g1    Study#4    1  g1 200     Scen2       161 1840.7538  999  999    999
## 5_g1    Study#5    1  g1 200     Scen2       162 1605.1504  999  999    999
## 6_g1    Study#6    1  g1 200     Scen2       164 1496.5477  999  999    999
## 7_g1    Study#7    1  g1 200     Scen2       161 1622.6838  999  999    999
## 8_g1    Study#8    1  g1 200     Scen2       162 1575.8092  999  999    999
## 9_g1    Study#9    1  g1 200     Scen2       161 1638.6499  999  999    999
## 10_g1  Study#10    0  g1 200     Scen2       200  439.5240  999  999    999
## 1_g2    Study#1    1  g2 200     Scen2       199  723.4652  999  999    999
## 2_g2    Study#2    1  g2 200     Scen2       198  725.3088  999  999    999
## 3_g2    Study#3    1  g2 200     Scen2       200  633.6027  999  999    999
## 4_g2    Study#4    1  g2 200     Scen2       199  631.2705  999  999    999
## 5_g2    Study#5    1  g2 200     Scen2       198  701.9784  999  999    999
## 6_g2    Study#6    1  g2 200     Scen2       196  705.4184  999  999    999
## 7_g2    Study#7    1  g2 200     Scen2       199  680.0606  999  999    999
## 8_g2    Study#8    1  g2 200     Scen2       198  704.2055  999  999    999
## 9_g2    Study#9    1  g2 200     Scen2       199  727.2699  999  999    999
## 10_g2  Study#10    0  g2 200     Scen2       160 3910.1011  999  999    999
##         TREAT
## 1_g1    Scen2
## 2_g1    Scen2
## 3_g1    Scen2
## 4_g1    Scen2
## 5_g1    Scen2
## 6_g1    Scen2
## 7_g1    Scen2
## 8_g1    Scen2
## 9_g1    Scen2
## 10_g1   Scen2
```

```
## 1_g2  Scen2
## 2_g2  Scen2
## 3_g2  Scen2
## 4_g2  Scen2
## 5_g2  Scen2
## 6_g2  Scen2
## 7_g2  Scen2
## 8_g2  Scen2
## 9_g2  Scen2
## 10_g2 Scen2
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                                  csv group            analysis saf_topic
## Strong Prior Data Conflict Scen02.csv   g1 Incidence proportion   Scen02
##                             seed pool      tau  heterog  ESS rob_weight
## Strong Prior Data Conflict 1701611344 TRUE HalfNormal Moderate elir        0.8
##                             nta_event nta_npat
## Strong Prior Data Conflict       199      200
```

Characteristic	Lower Threshold	Upper Threshold
log Expected MAP Prior: mean	-2.30054445698096	-2.29569754639357
log Expected MAP Prior: SD	0.045703431102168	0.0522282054683739
log Expected MAP Prior: median	-2.30071213719161	-2.29563974573589
log 95% CrILB	-2.40847499558611	-2.38644119833248
log 95% CrIUB	-2.208998796162	-2.1890158663589
log ESS	499.991756491329	2970263.27310499
log Expected robustified MAP Prior: mean	-0.151788891396192	-0.150819509278714
log Expected robustified MAP Prior: SD	1.39663448897852	1.39812904029192
log Expected robustified MAP Prior: median	0.066730434542889	0.0667936943460765
log 95% CrILB	-2.3542423011039	-2.34548216611581
log 95% CrIUB	2.24813243487503	2.2481326916657
log ESS	97.9195586700853	538510.697068051
log Expected results for Likelihood: mean	-0.951657875711446	-0.951657875711446
log Expected results for Likelihood: SD	0.0707106781186548	0.0707106781186548
log Expected results for Likelihood: median	-0.951657875711446	-0.951657875711446
log 95% CrILB	-1.09024825814641	-1.09024825814641
log 95% CrIUB	-0.813067493276479	-0.813067493276479
log ESS	NA	NA
log Expected results for Posterior: mean	-0.945005846980006	-0.945005846479051
log Expected results for Posterior: SD	0.0705345615858597	0.0705345620319703
log Expected results for Posterior: median	-0.945036226649493	-0.94497639790984
log 95% CrILB	-1.08326708600081	-1.08324474932306
log 95% CrIUB	-0.806791135755281	-0.806730117313984
log ESS	NA	NA
exp Expected MAP Prior: mean	0.100324209369122	0.100808000626919
exp Expected MAP Prior: SD	0.00459740324970764	0.00528285880063611
exp Expected MAP Prior: median	0.100187471089211	0.100696952345733
exp 95% CrILB	0.0899523678979051	0.0919563567020145

Characteristic	Lower Threshold	Upper Threshold
exp 95% CrIUB	0.109810536251905	0.112026943879775
exp ESS	NA	NA
exp Expected robustified MAP Prior: mean	0.100324209369122	0.100808000626919
exp Expected robustified MAP Prior: SD	0.00459740324970764	0.00528285880063611
exp Expected robustified MAP Prior: median	0.100187471089211	0.100696952345733
exp 95% CrILB	0.0899523678979051	0.0919563567020145
exp 95% CrIUB	0.109810536251905	0.112026943879775
exp ESS	NA	NA
exp Expected results for Likelihood: mean	NA	NA
exp Expected results for Likelihood: SD	NA	NA
exp Expected results for Likelihood: median	NA	NA
exp 95% CrILB	NA	NA
exp 95% CrIUB	NA	NA
exp ESS	NA	NA
exp Expected results for Posterior: mean	0.389366790587675	0.389935569628413
exp Expected results for Posterior: SD	0.0273264127982123	0.0277178576232242
exp Expected results for Posterior: median	0.38829463090252	0.389011858202018
exp 95% CrILB	0.337828802098825	0.339143270357254
exp 95% CrIUB	0.445514533629447	0.447321185404224
exp ESS	NA	NA

6.2.3 Scenario 3 - Realistic Scenario

Scenario 3 describes a binary endpoint for a realistic situation with a dropout rate of 5%, some with a 2% tau, events observed at a 90% power, homogeneous historical data and with no planned prior data conflict.

```
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0.05, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 93,
  SimStudy_censor_type = 2,
  nStudy = 6,
  tau = 0.02,
  prior_data_conflict = FALSE,
  pdc_hz = NA,
  SAF_TOPIC = "Scen3",
  seed = 1701621384
)
```

```
##       STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE  TOT_EXP DOSE FREQ LENGTH TREAT
## 1_g1 Study#1    1  g1 200     Scen3        30 282.8273  999  999    999 Scen3
## 2_g1 Study#2    1  g1 200     Scen3        35 345.5776  999  999    999 Scen3
## 3_g1 Study#3    1  g1 200     Scen3        32 355.6786  999  999    999 Scen3
## 4_g1 Study#4    1  g1 200     Scen3        35 409.5392  999  999    999 Scen3
```

```
## 5_g1 Study#5   1  g1 200      Scen3      36 207.1725  999  999    999 Scen3
## 6_g1 Study#6   0  g1 200      Scen3      40 291.3027  999  999    999 Scen3
## 1_g2 Study#1   1  g2 200      Scen3      60 259.6821  999  999    999 Scen3
## 2_g2 Study#2   1  g2 200      Scen3      52 268.0612  999  999    999 Scen3
## 3_g2 Study#3   1  g2 200      Scen3      57 237.5458  999  999    999 Scen3
## 4_g2 Study#4   1  g2 200      Scen3      54 359.4474  999  999    999 Scen3
## 5_g2 Study#5   1  g2 200      Scen3      52 170.1687  999  999    999 Scen3
## 6_g2 Study#6   0  g2 200      Scen3      50 266.0703  999  999    999 Scen3
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                        csv group       analysis saf_topic     seed
## Realisitic Scenarios Scen03.csv  g1 Incidence proportion   Scen03 1701621384
##                      pool     tau    heterog  ESS rob_weight nta_event
## Realisitic Scenarios TRUE HalfNormal Substantial elir       0.25        31
##                      nta_npat
## Realisitic Scenarios     200
```

Characteristic	Lower Threshold	Upper Threshold
log Expected MAP Prior: mean	-2.30253515121507	-2.2721715469521
log Expected MAP Prior: SD	0.252398825519465	0.29102807923359
log Expected MAP Prior: median	-2.31318741346349	-2.28056835868876
log 95% CrILB	-2.88653653224281	-2.78460704990026
log 95% CrIUB	-1.77149740387182	-1.63362420080078
log ESS	17.4893123665611	23.6294030160632
log Expected robustified MAP Prior: mean	-1.7033013634113	-1.68052866021407
log Expected robustified MAP Prior: SD	1.16457604225182	1.17637336266364
log Expected robustified MAP Prior: median	-2.22412872998234	-2.19192949010786
log 95% CrILB	-2.85175198014794	-2.75052437969524
log 95% CrIUB	1.37592111726956	1.37601783933676
log ESS	12.6692611860919	17.2804294861003
log Expected results for Likelihood: mean	-2.3604583050683	-2.3604583050683
log Expected results for Likelihood: SD	0.179605302026775	0.179605302026775
log Expected results for Likelihood: median	-2.3604583050683	-2.3604583050683
log 95% CrILB	-2.71247822847321	-2.71247822847321
log 95% CrIUB	-2.00843838166338	-2.00843838166338
log ESS	NA	NA
log Expected results for Posterior: mean	-2.33765776307338	-2.32252183060267
log Expected results for Posterior: SD	0.126604573972521	0.135362312413632
log Expected results for Posterior: median	-2.33749556933233	-2.31954087380735
log 95% CrILB	-2.60685442212831	-2.5828216286794
log 95% CrIUB	-2.08352662477966	-2.06562533927917
log ESS	NA	NA
exp Expected MAP Prior: mean	0.10364395533743	0.107279251623736
exp Expected MAP Prior: SD	0.0284929262149573	0.0503543578952479
exp Expected MAP Prior: median	0.0989453687288475	0.102226089669455
exp 95% CrILB	0.0557690341770198	0.0617533506163129
exp 95% CrIUB	0.170078136852588	0.195220771510104
exp ESS	NA	NA
exp Expected robustified MAP Prior: mean	0.10364395533743	0.107279251623736

Characteristic	Lower Threshold	Upper Threshold
exp Expected robustified MAP Prior: SD	0.0284929262149573	0.0503543578952479
exp Expected robustified MAP Prior: median	0.0989453687288475	0.102226089669455
exp 95% CrILB	0.0557690341770198	0.0617533506163129
exp 95% CrIUB	0.170078136852588	0.195220771510104
exp ESS	NA	NA
exp Expected results for Likelihood: mean	NA	NA
exp Expected results for Likelihood: SD	NA	NA
exp Expected results for Likelihood: median	NA	NA
exp 95% CrILB	NA	NA
exp 95% CrIUB	NA	NA
exp ESS	NA	NA
exp Expected results for Posterior: mean	0.0973775610168458	0.0989029743195379
exp Expected results for Posterior: SD	0.0123734341562885	0.0133418203726036
exp Expected results for Posterior: median	0.0965398693765347	0.0983384243251796
exp 95% CrILB	0.0735534363115164	0.0756465229193627
exp 95% CrIUB	0.124430194400045	0.126885382317147
exp ESS	NA	NA

6.2.4 Scenario 4 - Worst Case Scenario

Scenario 4 describes a binary endpoint for a worst case scenario with huge censoring during the trial, huge noise in the data, low number of events observed at 90% power, heterogeneous historical data and huge data conflict.

```
SimTestData(
  SimStudy_nPat = c(g1 = 50, g2 = 100),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0.2, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 112,
  SimStudy_censor_type = 2,
  nStudy = 3,
  tau = 0.15,
  prior_data_conflict = TRUE,
  pdc_hz = c(g1 = 0.05, g2 = 0.1),
  SAF_TOPIC = "Scen4",
  seed = 1701626683
)
```

```
##       STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE  TOT_EXP DOSE FREQ LENGTH TREAT
## 1_g1 Study#1    1  g1  50     Scen4        28 197.5691  999  999    999 Scen4
## 2_g1 Study#2    1  g1  50     Scen4        27 237.3923  999  999    999 Scen4
## 3_g1 Study#3    0  g1  50     Scen4        23 425.0280  999  999    999 Scen4
## 1_g2 Study#1    1  g2 100     Scen4        73 283.1671  999  999    999 Scen4
## 2_g2 Study#2    1  g2 100     Scen4        73 334.8827  999  999    999 Scen4
## 3_g2 Study#3    0  g2 100     Scen4        70 750.5857  999  999    999 Scen4
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                          csv group        analysis saf_topic        seed
## Worst Case Scenario Scen04.csv   g1 Incidence proportion    Scen04 1701626683
##                     pool        tau    heterog  ESS rob_weight nta_event
## Worst Case Scenario TRUE HalfNormal Very Large elir       0.99        27
##                     nta_npat
## Worst Case Scenario       50
```

Characteristic	Lower Threshold	Upper Threshold
log Expected MAP Prior: mean	NA	NA
log Expected MAP Prior: SD	NA	NA
log Expected MAP Prior: median	NA	NA
log 95% CrILB	NA	NA
log 95% CrIUB	NA	NA
log ESS	NA	NA
log Expected robustified MAP Prior: mean	NA	NA
log Expected robustified MAP Prior: SD	NA	NA
log Expected robustified MAP Prior: median	NA	NA
log 95% CrILB	NA	NA
log 95% CrIUB	NA	NA
log ESS	NA	NA
log Expected results for Likelihood: mean	NA	NA
log Expected results for Likelihood: SD	NA	NA
log Expected results for Likelihood: median	NA	NA
log 95% CrILB	NA	NA
log 95% CrIUB	NA	NA
log ESS	NA	NA
log Expected results for Posterior: mean	NA	NA
log Expected results for Posterior: SD	NA	NA
log Expected results for Posterior: median	NA	NA
log 95% CrILB	NA	NA
log 95% CrIUB	NA	NA
log ESS	NA	NA
exp Expected MAP Prior: mean	NA	NA
exp Expected MAP Prior: SD	NA	NA
exp Expected MAP Prior: median	NA	NA
exp 95% CrILB	NA	NA
exp 95% CrIUB	NA	NA
exp ESS	NA	NA
exp Expected robustified MAP Prior: mean	NA	NA
exp Expected robustified MAP Prior: SD	NA	NA
exp Expected robustified MAP Prior: median	NA	NA
exp 95% CrILB	NA	NA
exp 95% CrIUB	NA	NA
exp ESS	NA	NA
exp Expected results for Likelihood: mean	NA	NA
exp Expected results for Likelihood: SD	NA	NA
exp Expected results for Likelihood: median	NA	NA
exp 95% CrILB	NA	NA

Characteristic	Lower Threshold	Upper Threshold
exp 95% CrIUB	NA	NA
exp ESS	NA	NA
exp Expected results for Posterior: mean	NA	NA
exp Expected results for Posterior: SD	NA	NA
exp Expected results for Posterior: median	NA	NA
exp 95% CrILB	NA	NA
exp 95% CrIUB	NA	NA
exp ESS	NA	NA

6.2.5 Scenario 5 - Heterogeneous Data(Medium)

Scenario 5 describes a binary endpoint for a medium heterogenous scenario between the historical data, moderate noise at a 5% tau, moderate censoring at 5%, all events observed at a 90%power and no planned prior data conflict.

```
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0.05, time = 12),
  SimStudy_accr = 1,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 93,
  SimStudy_censor_type = 2,
  nStudy = 6,
  tau = 0.05,
  prior_data_conflict = FALSE,
  pdc_hz = NA,
  SAF_TOPIC = "Scen5",
  seed = 1701628373
)
```

```
##       STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE   TOT_EXP DOSE FREQ LENGTH TREAT
## 1_g1 Study#1    1  g1 200     Scen5        24 336.2761  999  999    999 Scen5
## 2_g1 Study#2    1  g1 200     Scen5        35 328.5856  999  999    999 Scen5
## 3_g1 Study#3    1  g1 200     Scen5        26 319.0432  999  999    999 Scen5
## 4_g1 Study#4    1  g1 200     Scen5        36 319.4839  999  999    999 Scen5
## 5_g1 Study#5    1  g1 200     Scen5        39 282.5063  999  999    999 Scen5
## 6_g1 Study#6    0  g1 200     Scen5        25 289.3660  999  999    999 Scen5
## 1_g2 Study#1    1  g2 200     Scen5        68 295.3881  999  999    999 Scen5
## 2_g2 Study#2    1  g2 200     Scen5        55 310.0651  999  999    999 Scen5
## 3_g2 Study#3    1  g2 200     Scen5        63 290.2667  999  999    999 Scen5
## 4_g2 Study#4    1  g2 200     Scen5        54 288.7203  999  999    999 Scen5
## 5_g2 Study#5    1  g2 200     Scen5        52 283.8704  999  999    999 Scen5
## 6_g2 Study#6    0  g2 200     Scen5        66 263.6880  999  999    999 Scen5
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                           csv group         analysis saf_topic       seed
## Heterogenous Data   Scen05.csv   g1 Incidence proportion    Scen05 1701628373
##                           pool      tau heterog  ESS rob_weight nta_event nta_npat
## Heterogenous Data   TRUE HalfNormal   Large elir       0.4        25       200
```

Characteristic	Lower Threshold	Upper Threshold
log Expected MAP Prior: mean	-2.27036204001293	-2.22606439938237
log Expected MAP Prior: SD	0.31173288078447	0.438878067193539
log Expected MAP Prior: median	-2.28077658176299	-2.25530307006346
log 95% CrILB	-2.98618506871448	-2.83916860677418
log 95% CrIUB	-1.61576638983349	-1.14928096202277
log ESS	14.0721747280866	20.3495925601282
log Expected robustified MAP Prior: mean	-1.79898963201035	-1.7635515195059
log Expected robustified MAP Prior: SD	1.07314392825347	1.09987512914229
log Expected robustified MAP Prior: median	-2.21749487231713	-2.18033786066382
log 95% CrILB	-2.94595327981259	-2.81449253459337
log 95% CrIUB	1.2368366416653	1.24340451169618
log ESS	10.8735558737914	15.9096243918136
log Expected results for Likelihood: mean	-2.44755086324423	-2.44755086324423
log Expected results for Likelihood: SD	0.2	0.2
log Expected results for Likelihood: median	-2.44755086324423	-2.44755086324423
log 95% CrILB	-2.83954366015224	-2.83954366015224
log 95% CrIUB	-2.05555806633622	-2.05555806633622
log ESS	NA	NA
log Expected results for Posterior: mean	-2.37654276801164	-2.35735165001093
log Expected results for Posterior: SD	0.144088704451342	0.154480158247438
log Expected results for Posterior: median	-2.37504431320554	-2.34880495732956
log 95% CrILB	-2.69623000961166	-2.65938681237547
log 95% CrIUB	-2.09614667373703	-2.07405870091687
log ESS	NA	NA
exp Expected MAP Prior: mean	0.109088403682114	0.127034849846526
exp Expected MAP Prior: SD	0.0397866741463018	0.223053381801413
exp Expected MAP Prior: median	0.10220480551693	0.104841764560528
exp 95% CrILB	0.0504796475480942	0.0584742692207235
exp 95% CrIUB	0.198738485912578	0.316864666013624
exp ESS	NA	NA
exp Expected robustified MAP Prior: mean	0.109088403682114	0.127034849846526
exp Expected robustified MAP Prior: SD	0.0397866741463018	0.223053381801413
exp Expected robustified MAP Prior: median	0.10220480551693	0.104841764560528
exp 95% CrILB	0.0504796475480942	0.0584742692207235
exp 95% CrIUB	0.198738485912578	0.316864666013624
exp ESS	NA	NA
exp Expected results for Likelihood: mean	NA	NA
exp Expected results for Likelihood: SD	NA	NA
exp Expected results for Likelihood: median	NA	NA
exp 95% CrILB	NA	NA
exp 95% CrIUB	NA	NA
exp ESS	NA	NA
exp Expected results for Posterior: mean	0.0939165658567678	0.0957485671299483
exp Expected results for Posterior: SD	0.0134951897955422	0.0146133477585285

Characteristic	Lower Threshold	Upper Threshold
exp Expected results for Posterior: median	0.0930114785160412	0.0955112695350595
exp 95% CrILB	0.0673628923698803	0.0701178931707269
exp 95% CrIUB	0.122874752300526	0.125846489860166
exp ESS	NA	NA

6.2.6 Scenario 6 - High Dropout

Scenario 6 describes a binary endpoint scenario with huge dropout within the current trial, some noise at a 2% tau, some event being observed at a 90% power, homogeneous data and no planned prior data conflict.

```
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0.3, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 95,
  SimStudy_censor_type = 2,
  nStudy = 6,
  tau = 0.02,
  prior_data_conflict = FALSE,
  pdc_hz = NA,
  SAF_TOPIC = "Scen6",
  seed = 1701628373
)
```

```
##        STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE  TOT_EXP DOSE FREQ LENGTH TREAT
## 1_g1 Study#1    1  g1 200     Scen6        26 291.6589  999  999    999 Scen6
## 2_g1 Study#2    1  g1 200     Scen6        27 225.3005  999  999    999 Scen6
## 3_g1 Study#3    1  g1 200     Scen6        28 292.3146  999  999    999 Scen6
## 4_g1 Study#4    1  g1 200     Scen6        28 268.4692  999  999    999 Scen6
## 5_g1 Study#5    1  g1 200     Scen6        40 212.6690  999  999    999 Scen6
## 6_g1 Study#6    0  g1 200     Scen6        24 198.0645  999  999    999 Scen6
## 1_g2 Study#1    1  g2 200     Scen6        56 226.4060  999  999    999 Scen6
## 2_g2 Study#2    1  g2 200     Scen6        52 203.6631  999  999    999 Scen6
## 3_g2 Study#3    1  g2 200     Scen6        55 255.6490  999  999    999 Scen6
## 4_g2 Study#4    1  g2 200     Scen6        47 221.9167  999  999    999 Scen6
## 5_g2 Study#5    1  g2 200     Scen6        45 238.6339  999  999    999 Scen6
## 6_g2 Study#6    0  g2 200     Scen6        54 219.5831  999  999    999 Scen6
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                     csv group          analysis saf_topic      seed pool
## High Dropout Scen06.csv    g1 Incidence proportion    Scen06 1701628373 TRUE
```

```
##                          tau  heterog  ESS rob_weight nta_event nta_npat
## High Dropout HalfNormal Moderate elir         0.14        31       200
```

Characteristic	Lower Threshold	Upper Threshold
log Expected MAP Prior: mean	-2.14571075047067	-2.12581284512846
log Expected MAP Prior: SD	0.185430962323633	0.207119249955804
log Expected MAP Prior: median	-2.14923642103297	-2.12851233128213
log 95% CrILB	-2.57733430588538	-2.50141751168368
log 95% CrIUB	-1.76454156972802	-1.67130471589967
log ESS	28.9672898500887	37.0775849945859
log Expected robustified MAP Prior: mean	-1.82845524540477	-1.81134304681047
log Expected robustified MAP Prior: SD	0.883953794601911	0.89041613103786
log Expected robustified MAP Prior: median	-2.11708925201342	-2.09685061563857
log 95% CrILB	-2.56063045562642	-2.49389981542061
log 95% CrIUB	1.04122402113669	1.04124033845178
log ESS	24.3891440769273	31.2842060000024
log Expected results for Likelihood: mean	-2.11508888041007	-2.11508888041007
log Expected results for Likelihood: SD	0.179605302026775	0.179605302026775
log Expected results for Likelihood: median	-2.11508888041007	-2.11508888041007
log 95% CrILB	-2.46710880381499	-2.46710880381499
log 95% CrIUB	-1.76306895700516	-1.76306895700516
log ESS	NA	NA
log Expected results for Posterior: mean	-2.1344521718923	-2.1230908245444
log Expected results for Posterior: SD	0.11584317562596	0.123136734859324
log Expected results for Posterior: median	-2.1369457863246	-2.12337796359474
log 95% CrILB	-2.37255601966837	-2.35400354917435
log 95% CrIUB	-1.89771235217365	-1.87586451444203
log ESS	NA	NA
exp Expected MAP Prior: mean	0.119285988991372	0.121781806522033
exp Expected MAP Prior: SD	0.0227407111900856	0.0277810335574208
exp Expected MAP Prior: median	0.116573136642813	0.119014216146037
exp 95% CrILB	0.0759762638145918	0.0819687267149617
exp 95% CrIUB	0.171265287863463	0.188001630981805
exp ESS	NA	NA
exp Expected robustified MAP Prior: mean	0.119285988991372	0.121781806522033
exp Expected robustified MAP Prior: SD	0.0227407111900856	0.0277810335574208
exp Expected robustified MAP Prior: median	0.116573136642813	0.119014216146037
exp 95% CrILB	0.0759762638145918	0.0819687267149617
exp 95% CrIUB	0.171265287863463	0.188001630981805
exp ESS	NA	NA
exp Expected results for Likelihood: mean	NA	NA
exp Expected results for Likelihood: SD	NA	NA
exp Expected results for Likelihood: median	NA	NA
exp 95% CrILB	NA	NA
exp 95% CrIUB	NA	NA
exp ESS	NA	NA
exp Expected results for Posterior: mean	0.119142063719417	0.120589743438264
exp Expected results for Posterior: SD	0.0139861185661857	0.0148841524761785
exp Expected results for Posterior: median	0.118049710723537	0.119686030590554
exp 95% CrILB	0.0931295877922723	0.0951885953564295
exp 95% CrIUB	0.149843717914155	0.153377691999342
exp ESS	NA	NA

6.2.7 Scenario 7 - High Heterogeneity

Scenario 7 describes a binary endpoint scenario with high heterogeneity between historical data, moderate censoring in current trial, moderate noise at a 2% tau, all events observed at a 90% power, with no planned prior data conflict.

```
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0.05, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 93,
  SimStudy_censor_type = 2,
  nStudy = 6,
  tau = 0.15,
  prior_data_conflict = FALSE,
  pdc_hz = NA,
  SAF_TOPIC = "Scen7",
  seed = 1701416989
)
```

```
##        STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE    TOT_EXP DOSE FREQ LENGTH TREAT
## 1_g1 Study#1    1  g1 200     Scen7        32 222.47360  999  999    999 Scen7
## 2_g1 Study#2    1  g1 200     Scen7        27 270.34094  999  999    999 Scen7
## 3_g1 Study#3    1  g1 200     Scen7        32 271.08747  999  999    999 Scen7
## 4_g1 Study#4    1  g1 200     Scen7        36 116.93497  999  999    999 Scen7
## 5_g1 Study#5    1  g1 200     Scen7        29 111.37228  999  999    999 Scen7
## 6_g1 Study#6    0  g1 200     Scen7        23 163.68689  999  999    999 Scen7
## 1_g2 Study#1    1  g2 200     Scen7        59 189.49417  999  999    999 Scen7
## 2_g2 Study#2    1  g2 200     Scen7        62 284.62991  999  999    999 Scen7
## 3_g2 Study#3    1  g2 200     Scen7        58 210.80011  999  999    999 Scen7
## 4_g2 Study#4    1  g2 200     Scen7        56  77.53109  999  999    999 Scen7
## 5_g2 Study#5    1  g2 200     Scen7        62 118.22857  999  999    999 Scen7
## 6_g2 Study#6    0  g2 200     Scen7        68  97.68813  999  999    999 Scen7
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                          csv group           analysis saf_topic       seed
## High Heterogeneity Scen07.csv   g1 Incidence proportion    Scen07 1701416989
##                         pool      tau    heterog  ESS rob_weight nta_event
## High Heterogeneity TRUE HalfNormal Very Large elir        0.2        35
##                    nta_npat
## High Heterogeneity      200
```

Characteristic	Lower Threshold	Upper Threshold
log Expected MAP Prior: mean	-1.67787693207814	-1.60516715848896
log Expected MAP Prior: SD	0.713835169880213	0.808040122600875
log Expected MAP Prior: median	-1.71632237897338	-1.64215604979272
log 95% CrILB	-3.22457628045853	-2.93612339560652
log 95% CrIUB	-0.143170207633716	0.238279625191639
log ESS	2.039159835701	424.113393954689
log Expected robustified MAP Prior: mean	-1.30430154566251	-1.24613372679117
log Expected robustified MAP Prior: SD	1.07145779488557	1.12327097135512
log Expected robustified MAP Prior: median	-1.54758613079677	-1.46677832958047
log 95% CrILB	-3.11844666428484	-2.88561864851411
log 95% CrIUB	1.35438210721229	1.45925092330396
log ESS	1.43507479743671	339.088969517844
log Expected results for Likelihood: mean	-1.74296930505862	-1.74296930505862
log Expected results for Likelihood: SD	0.169030850945703	0.169030850945703
log Expected results for Likelihood: median	-1.74296930505862	-1.74296930505862
log 95% CrILB	-2.07426368518836	-2.07426368518836
log 95% CrIUB	-1.41167492492889	-1.41167492492889
log ESS	NA	NA
log Expected results for Posterior: mean	-1.74564670866854	-1.73328912841804
log Expected results for Posterior: SD	0.158046481523802	0.163065598285613
log Expected results for Posterior: median	-1.7463739485189	-1.73300208669544
log 95% CrILB	-2.06015241140477	-2.04740507377882
log 95% CrIUB	-1.43093989277468	-1.41652166751234
log ESS	NA	NA
exp Expected MAP Prior: mean	0.253035317559884	5.71719465841664
exp Expected MAP Prior: SD	0.326492862490418	344.180710243076
exp Expected MAP Prior: median	0.179725900945171	0.193562262243659
exp 95% CrILB	0.0397726856325538	0.0530711248423622
exp 95% CrIUB	0.866606554256365	1.26906470915605
exp ESS	NA	NA
exp Expected robustified MAP Prior: mean	0.253035317559884	5.71719465841664
exp Expected robustified MAP Prior: SD	0.326492862490418	344.180710243076
exp Expected robustified MAP Prior: median	0.179725900945171	0.193562262243659
exp 95% CrILB	0.0397726856325538	0.0530711248423622
exp 95% CrIUB	0.866606554256365	1.26906470915605
exp ESS	NA	NA
exp Expected results for Likelihood: mean	NA	NA
exp Expected results for Likelihood: SD	NA	NA
exp Expected results for Likelihood: median	NA	NA
exp 95% CrILB	NA	NA
exp 95% CrIUB	NA	NA
exp ESS	NA	NA
exp Expected results for Posterior: mean	0.176799333766977	0.179139461159602
exp Expected results for Posterior: SD	0.0282180081275081	0.0293656175695681
exp Expected results for Posterior: median	0.174338346870683	0.176839044922285
exp 95% CrILB	0.127263753708629	0.129245964473556
exp 95% CrIUB	0.238888373435222	0.242924940709672
exp ESS	NA	NA

6.2.8 Scenario 8 - Bad Scenario

Scenario 8 describes a binary endpoint for a bad scenario with huge censoring in the current trial, huge noise, little events observed in the current trial, heterogeneous historical data and no planned prior data conflict.

```
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0.3, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 93,
  SimStudy_censor_type = 2,
  nStudy = 6,
  tau = 0.15,
  prior_data_conflict = FALSE,
  pdc_hz = NA,
  SAF_TOPIC = "Scen8",
  seed = 1701652217
)
```

```
##        STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE  TOT_EXP DOSE FREQ LENGTH TREAT
## 1_g1 Study#1    1  g1 200     Scen8        22 297.7669  999  999    999 Scen8
## 2_g1 Study#2    1  g1 200     Scen8        31 298.1832  999  999    999 Scen8
## 3_g1 Study#3    1  g1 200     Scen8        21 307.9312  999  999    999 Scen8
## 4_g1 Study#4    1  g1 200     Scen8        21 379.2739  999  999    999 Scen8
## 5_g1 Study#5    1  g1 200     Scen8        28 405.2051  999  999    999 Scen8
## 6_g1 Study#6    0  g1 200     Scen8        30 368.8481  999  999    999 Scen8
## 1_g2 Study#1    1  g2 200     Scen8        53 234.0924  999  999    999 Scen8
## 2_g2 Study#2    1  g2 200     Scen8        45 226.9392  999  999    999 Scen8
## 3_g2 Study#3    1  g2 200     Scen8        55 211.8717  999  999    999 Scen8
## 4_g2 Study#4    1  g2 200     Scen8        56 348.7668  999  999    999 Scen8
## 5_g2 Study#5    1  g2 200     Scen8        46 375.9676  999  999    999 Scen8
## 6_g2 Study#6    0  g2 200     Scen8        45 284.3348  999  999    999 Scen8
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                      csv group          analysis saf_topic       seed pool
## Bad Scenario Scen08.csv    g1 Incidence proportion    Scen08 1701652217 TRUE
##                      tau heterog  ESS rob_weight nta_event nta_npat
## Bad Scenario HalfNormal  Large elir      0.2          25      200
```

Characteristic	Lower Threshold	Upper Threshold
log Expected MAP Prior: mean	-2.58923732694738	-2.54487981664089
log Expected MAP Prior: SD	0.272441281275459	0.376079630571757

Characteristic	Lower Threshold	Upper Threshold
log Expected MAP Prior: median	-2.6009605878439	-2.57482032343642
log 95% CrILB	-3.22630923846181	-3.09328030340787
log 95% CrIUB	-2.00077807783612	-1.65125574328735
log ESS	19.0724163671423	25.4899538233109
log Expected robustified MAP Prior: mean	-2.0565698615579	-2.02108385331271
log Expected robustified MAP Prior: SD	1.17506618223914	1.18991182897732
log Expected robustified MAP Prior: median	-2.53994249189765	-2.50910964236525
log 95% CrILB	-3.19402666403271	-3.0689716733129
log 95% CrIUB	1.22441959885731	1.22766649298823
log ESS	15.0685205583812	20.207402836359
log Expected results for Likelihood: mean	-2.2676978339936	-2.2676978339936
log Expected results for Likelihood: SD	0.169030850945703	0.169030850945703
log Expected results for Likelihood: median	-2.2676978339936	-2.2676978339936
log 95% CrILB	-2.59899221412334	-2.59899221412334
log 95% CrIUB	-1.93640345386387	-1.93640345386387
log ESS	NA	NA
log Expected results for Posterior: mean	-2.40585951153042	-2.38299616863632
log Expected results for Posterior: SD	0.141564073469474	0.159244217389157
log Expected results for Posterior: median	-2.41914475555867	-2.39515551802918
log 95% CrILB	-2.66352569841375	-2.65061176080451
log 95% CrIUB	-2.08695006130757	-2.04801905735462
log ESS	NA	NA
exp Expected MAP Prior: mean	0.0783269051789089	0.0877618323729666
exp Expected MAP Prior: SD	0.0257088250014225	0.274673784662625
exp Expected MAP Prior: median	0.0742022662715114	0.0761675073092984
exp 95% CrILB	0.0397037658906003	0.0453529417609483
exp 95% CrIUB	0.135230025858622	0.19180891118861
exp ESS	NA	NA
exp Expected robustified MAP Prior: mean	0.0783269051789089	0.0877618323729666
exp Expected robustified MAP Prior: SD	0.0257088250014225	0.274673784662625
exp Expected robustified MAP Prior: median	0.0742022662715114	0.0761675073092984
exp 95% CrILB	0.0397037658906003	0.0453529417609483
exp 95% CrIUB	0.135230025858622	0.19180891118861
exp ESS	NA	NA
exp Expected results for Likelihood: mean	NA	NA
exp Expected results for Likelihood: SD	NA	NA
exp Expected results for Likelihood: median	NA	NA
exp 95% CrILB	NA	NA
exp 95% CrIUB	NA	NA
exp ESS	NA	NA
exp Expected results for Posterior: mean	0.0911120264038836	0.0934742870981482
exp Expected results for Posterior: SD	0.013518703088776	0.0153307735207302
exp Expected results for Posterior: median	0.0890021685801336	0.0911884543626467
exp 95% CrILB	0.0697144810950481	0.0707489259260008
exp 95% CrIUB	0.124017529359014	0.129087653931431
exp ESS	NA	NA

6.2.9   Scenario 9 - Good Scenario

Scenario 9 describes a binary endpoint for a good scenario with low censoring in the current trial, small noise, majority of the events being observed and homogeneous historical data.

```
SimTestData(
  SimStudy_nPat = c(g1 = 300, g2 = 300),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 24,
  SimStudy_NObsEvt = 0.999,
  SimStudy_censor_type = 1,
  nStudy = 8,
  tau = 0.01,
  prior_data_conflict = FALSE,
  pdc_hz = NA,
  SAF_TOPIC = "Scen9",
  seed = 1701655293
)
```

```
##         STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE  TOT_EXP DOSE FREQ LENGTH TREAT
## 1_g1 Study#1    1  g1 300    Scen9       260 2838.989  999  999    999 Scen9
## 2_g1 Study#2    1  g1 300    Scen9       259 2624.533  999  999    999 Scen9
## 3_g1 Study#3    1  g1 300    Scen9       251 2933.272  999  999    999 Scen9
## 4_g1 Study#4    1  g1 300    Scen9       251 2984.729  999  999    999 Scen9
## 5_g1 Study#5    1  g1 300    Scen9       259 2667.259  999  999    999 Scen9
## 6_g1 Study#6    1  g1 300    Scen9       265 2774.955  999  999    999 Scen9
## 7_g1 Study#7    1  g1 300    Scen9       255 2665.750  999  999    999 Scen9
## 8_g1 Study#8    0  g1 300    Scen9       261 2691.265  999  999    999 Scen9
## 1_g2 Study#1    1  g2 300    Scen9       292 1550.852  999  999    999 Scen9
## 2_g2 Study#2    1  g2 300    Scen9       295 1646.227  999  999    999 Scen9
## 3_g2 Study#3    1  g2 300    Scen9       297 1360.433  999  999    999 Scen9
## 4_g2 Study#4    1  g2 300    Scen9       289 1676.768  999  999    999 Scen9
## 5_g2 Study#5    1  g2 300    Scen9       294 1678.219  999  999    999 Scen9
## 6_g2 Study#6    1  g2 300    Scen9       295 1628.496  999  999    999 Scen9
## 7_g2 Study#7    1  g2 300    Scen9       295 1628.708  999  999    999 Scen9
## 8_g2 Study#8    0  g2 300    Scen9       295 1486.654  999  999    999 Scen9
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                      csv group          analysis saf_topic        seed pool
## Good Scenario Scen09.csv    g1 Incidence proportion    Scen09 1701655293 TRUE
##                      tau heterog  ESS rob_weight nta_event nta_npat
## Good Scenario HalfNormal   Small elir      0.05       175      200
```

Characteristic	Lower Threshold	Upper Threshold
log Expected MAP Prior: mean	-2.38286031860573	-2.37773915683797
log Expected MAP Prior: SD	0.0477787043101146	0.0548418651039118
log Expected MAP Prior: median	-2.38293427836704	-2.37825968713331

Characteristic	Lower Threshold	Upper Threshold
log 95% CrILB	-2.49532668010869	-2.47475045305626
log 95% CrIUB	-2.28677814074689	-2.26060973441392
log ESS	497.240219038706	620.154948719205
log Expected robustified MAP Prior: mean	-2.25908730267544	-2.25422219899607
log Expected robustified MAP Prior: SD	0.58497940788604	0.586153194078693
log Expected robustified MAP Prior: median	-2.38023594195844	-2.37608823149858
log 95% CrILB	-2.50082603944329	-2.47519086501909
log 95% CrIUB	0.0925828632283981	0.0926229697919316
log ESS	471.807852248907	588.536285522549
log Expected results for Likelihood: mean	-2.3859667019331	-2.3859667019331
log Expected results for Likelihood: SD	0.104257207028539	0.104257207028539
log Expected results for Likelihood: median	-2.3859667019331	-2.3859667019331
log 95% CrILB	-2.59030707283777	-2.59030707283777
log 95% CrIUB	-2.18162633102843	-2.18162633102843
log ESS	NA	NA
log Expected results for Posterior: mean	-2.38322849949019	-2.37961762844177
log Expected results for Posterior: SD	0.0396401362120798	0.0429367013272133
log Expected results for Posterior: median	-2.38315216038299	-2.37961434309976
log 95% CrILB	-2.47243044761222	-2.46063474296863
log 95% CrIUB	-2.30285646841619	-2.28933531804462
log ESS	NA	NA
exp Expected MAP Prior: mean	0.0924050270446036	0.0928744868294921
exp Expected MAP Prior: SD	0.00441939979821955	0.00516612215050858
exp Expected MAP Prior: median	0.0922794064003049	0.0927117847063368
exp 95% CrILB	0.0824695061320551	0.0841839967683169
exp 95% CrIUB	0.1015932542998	0.104286878110824
exp ESS	NA	NA
exp Expected robustified MAP Prior: mean	0.0924050270446036	0.0928744868294921
exp Expected robustified MAP Prior: SD	0.00441939979821955	0.00516612215050858
exp Expected robustified MAP Prior: median	0.0922794064003049	0.0927117847063368
exp 95% CrILB	0.0824695061320551	0.0841839967683169
exp 95% CrIUB	0.1015932542998	0.104286878110824
exp ESS	NA	NA
exp Expected results for Likelihood: mean	NA	NA
exp Expected results for Likelihood: SD	NA	NA
exp Expected results for Likelihood: median	NA	NA
exp 95% CrILB	NA	NA
exp 95% CrIUB	NA	NA
exp ESS	NA	NA
exp Expected results for Posterior: mean	0.0923317252475515	0.0926825071485697
exp Expected results for Posterior: SD	0.00365420826874065	0.0039976371131795
exp Expected results for Posterior: median	0.0922566741985039	0.0925970753616474
exp 95% CrILB	0.0843727457171932	0.0854337713503067
exp 95% CrIUB	0.0999096103321246	0.101326422926439
exp ESS	NA	NA

6.2.10 Scenario 10 - Favoured Control

Scenario 10 describes a binary endpoint for a favored control scenario with no censoring in the current trial, no noise, all events being observed, homogeneous historical data, heavy prior data conflict and the hazard ratio in favor of the control group.

```
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.2, g2 = 0.1),
  SimStudy_dropout = c(rate = 0.05, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 93,
  SimStudy_censor_type = 2,
  nStudy = 6,
  tau = 0.02,
  prior_data_conflict = TRUE,
  pdc_hz = 1.2,
  SAF_TOPIC = "Scen10",
  seed = 1701673095
)
```

```
## Warning in rexp(nPat[i], hz[i]): NAs produced
```

```
##        STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE    TOT_EXP DOSE FREQ LENGTH
## 1_g1 Study#1    1  g1 200    Scen10        54 234.482445  999  999    999
## 2_g1 Study#2    1  g1 200    Scen10        42 200.954605  999  999    999
## 3_g1 Study#3    1  g1 200    Scen10        59 233.239862  999  999    999
## 4_g1 Study#4    1  g1 200    Scen10        51 204.363002  999  999    999
## 5_g1 Study#5    1  g1 200    Scen10        52 170.728016  999  999    999
## 6_g1 Study#6    0  g1 200    Scen10        93  -6.482995  999  999    999
## 1_g2 Study#1    1  g2 200    Scen10        36 282.421760  999  999    999
## 2_g2 Study#2    1  g2 200    Scen10        46 214.300246  999  999    999
## 3_g2 Study#3    1  g2 200    Scen10        32 318.335395  999  999    999
## 4_g2 Study#4    1  g2 200    Scen10        37 243.939964  999  999    999
## 5_g2 Study#5    1  g2 200    Scen10        39 244.166712  999  999    999
## 6_g2 Study#6    0  g2 200    Scen10        NA         NA  999  999    999
##        TREAT
## 1_g1 Scen10
## 2_g1 Scen10
## 3_g1 Scen10
## 4_g1 Scen10
## 5_g1 Scen10
## 6_g1 Scen10
## 1_g2 Scen10
## 2_g2 Scen10
## 3_g2 Scen10
## 4_g2 Scen10
## 5_g2 Scen10
## 6_g2 Scen10
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                       csv group        analysis saf_topic       seed pool
## Favored Control Scen10.csv   g1 Incidence proportion    Scen10 1701673095 TRUE
##                 tau heterog  ESS rob_weight nta_event nta_npat
## Favored Control HalfNormal   Small elir       0.6      175      200
```

Characteristic	Lower Threshold	Upper Threshold
log Expected MAP Prior: mean	-1.3978265988531	-1.38910830232281
log Expected MAP Prior: SD	0.0840701753189167	0.0924294216230324
log Expected MAP Prior: median	-1.39824902703698	-1.3885262500184
log 95% CrILB	-1.58375405322484	-1.55696865326308
log 95% CrIUB	-1.23652150979172	-1.19759153545227
log ESS	128.831004444722	154.533413749666
log Expected robustified MAP Prior: mean	-0.410810639541241	-0.407323320929125
log Expected robustified MAP Prior: SD	1.11604934307991	1.1192380951581
log Expected robustified MAP Prior: median	-0.720210132603968	-0.719563724921454
log 95% CrILB	-1.61654781628056	-1.58843525598759
log 95% CrIUB	1.97885528606121	1.97885528636148
log ESS	44.573361243809	54.2463489483615
log Expected results for Likelihood: mean	-0.287682072451781	-0.287682072451781
log Expected results for Likelihood: SD	0.0816496580927726	0.0816496580927726
log Expected results for Likelihood: median	-0.287682072451781	-0.287682072451781
log 95% CrILB	-0.447712461663625	-0.447712461663625
log 95% CrIUB	-0.127651683239937	-0.127651683239937
log ESS	NA	NA
log Expected results for Posterior: mean	-0.28415395938641	-0.284139807071306
log Expected results for Posterior: SD	0.0813788458771159	0.0813813984901243
log Expected results for Posterior: median	-0.284170304243161	-0.284109466158112
log 95% CrILB	-0.443669372439495	-0.44360900131585
log 95% CrIUB	-0.124654430244513	-0.124640350899231
log ESS	NA	NA
exp Expected MAP Prior: mean	0.248135146950455	0.250266615056984
exp Expected MAP Prior: SD	0.0209866803863799	0.0232963471631153
exp Expected MAP Prior: median	0.247029126808386	0.249442650067295
exp 95% CrILB	0.205203306614824	0.210774032948648
exp 95% CrIUB	0.290392590905577	0.301920503839205
exp ESS	NA	NA
exp Expected robustified MAP Prior: mean	0.248135146950455	0.250266615056984
exp Expected robustified MAP Prior: SD	0.0209866803863799	0.0232963471631153
exp Expected robustified MAP Prior: median	0.247029126808386	0.249442650067295
exp 95% CrILB	0.205203306614824	0.210774032948648
exp 95% CrIUB	0.290392590905577	0.301920503839205
exp ESS	NA	NA
exp Expected results for Likelihood: mean	NA	NA
exp Expected results for Likelihood: SD	NA	NA
exp Expected results for Likelihood: median	NA	NA
exp 95% CrILB	NA	NA
exp 95% CrIUB	NA	NA
exp ESS	NA	NA
exp Expected results for Posterior: mean	0.754560827635712	0.75575423723519
exp Expected results for Posterior: SD	0.0610622605977461	0.0620596767656557
exp Expected results for Posterior: median	0.751978766769221	0.753393123322098
exp 95% CrILB	0.640307759592105	0.643160211231947
exp 95% CrIUB	0.880997861992918	0.8845423498997

Characteristic	Lower Threshold	Upper Threshold
exp ESS	NA	NA

6.2.11 Scenario 11 - Continued study duration with Realistic Setting

Scenario 11 describes a binary endpoint for a realistic situation where the study continued regardless of when the proposed number of events has been observed. Characteristics of this scenario includes a drop out rate of 5%, noise at a 5% tau, homogeneous historical data and no planned prior data conflict planned.

```
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0.05, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 24,
  SimStudy_NObsEvt = 93,
  SimStudy_censor_type = 1,
  nStudy = 6,
  tau = 0.02,
  prior_data_conflict = FALSE,
  pdc_hz = NA,
  SAF_TOPIC = "Scen11",
  seed = 1701876972
)
```

```
##        STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE   TOT_EXP DOSE FREQ LENGTH  TREAT
## 1_g1 Study#1    1  g1 200    Scen11       170 1871.1930  999  999    999 Scen11
## 2_g1 Study#2    1  g1 200    Scen11       173 1630.1105  999  999    999 Scen11
## 3_g1 Study#3    1  g1 200    Scen11       168 1744.6636  999  999    999 Scen11
## 4_g1 Study#4    1  g1 200    Scen11       170 1904.9560  999  999    999 Scen11
## 5_g1 Study#5    1  g1 200    Scen11       166 1748.6775  999  999    999 Scen11
## 6_g1 Study#6    0  g1 200    Scen11       162 1879.6921  999  999    999 Scen11
## 1_g2 Study#1    1  g2 200    Scen11       191  910.6017  999  999    999 Scen11
## 2_g2 Study#2    1  g2 200    Scen11       192  957.8531  999  999    999 Scen11
## 3_g2 Study#3    1  g2 200    Scen11       196  922.9765  999  999    999 Scen11
## 4_g2 Study#4    1  g2 200    Scen11       198  927.3806  999  999    999 Scen11
## 5_g2 Study#5    1  g2 200    Scen11       193 1027.3669  999  999    999 Scen11
## 6_g2 Study#6    0  g2 200    Scen11       196 1068.8192  999  999    999 Scen11
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                                                         csv group
## Continued Study Duration with Realistic Setting Scen11.csv    g1
##                                                    analysis saf_topic
## Continued Study Duration with Realistic Setting Incidence proportion    Scen11
```

```
##                                              seed pool       tau
## Continued Study Duration with Realistic Setting 1701876972 TRUE HalfNormal
##                                            heterog  ESS rob_weight
## Continued Study Duration with Realistic Setting   Small elir       0.05
##                                            nta_event nta_npat
## Continued Study Duration with Realistic Setting       170      200
```

Characteristic	Lower Threshold	Upper Threshold
log Expected MAP Prior: mean	-2.35187014134489	-2.34580090097421
log Expected MAP Prior: SD	0.0588703890671759	0.065753185947754
log Expected MAP Prior: median	-2.35231036382262	-2.34531938951113
log 95% CrILB	-2.48989650601795	-2.46038717940403
log 95% CrIUB	-2.23480451451683	-2.20385749652879
log ESS	299.491844796247	1253127.20561646
log Expected robustified MAP Prior: mean	-2.29951663427764	-2.2237508559255
log Expected robustified MAP Prior: SD	0.580149097915129	0.581549504599843
log Expected robustified MAP Prior: median	-2.34873085885964	-2.34247028349435
log 95% CrILB	-2.49051495729235	-2.46055872095063
log 95% CrIUB	0.0951699569740826	0.0952259689363641
log ESS	284.138347260761	1177000.50567153
log Expected results for Likelihood: mean	-2.3538783873816	-2.3538783873816
log Expected results for Likelihood: SD	0.102597835208513	0.102597835208513
log Expected results for Likelihood: median	-2.3538783873816	-2.3538783873816
log 95% CrILB	-2.55496644928206	-2.55496644928206
log 95% CrIUB	-2.15279032548113	-2.15279032548113
log ESS	NA	NA
log Expected results for Posterior: mean	-2.35225515731827	-2.34790419985206
log Expected results for Posterior: SD	0.0467157223169838	0.0497729368395784
log Expected results for Posterior: median	-2.35238122744102	-2.34731524020139
log 95% CrILB	-2.45443660247532	-2.44039973788935
log 95% CrIUB	-2.26087235094644	-2.24820300324439
log ESS	NA	NA
exp Expected MAP Prior: mean	0.0953774051538436	0.0959501808208087
exp Expected MAP Prior: SD	0.00564423843111816	0.00636888483761372
exp Expected MAP Prior: median	0.095149079090347	0.0958165944634875
exp 95% CrILB	0.0829185477633717	0.0854018789276862
exp 95% CrIUB	0.107013048055469	0.110376559342516
exp ESS	NA	NA
exp Expected robustified MAP Prior: mean	0.0953774051538436	0.0959501808208087
exp Expected robustified MAP Prior: SD	0.00564423843111816	0.00636888483761372
exp Expected robustified MAP Prior: median	0.095149079090347	0.0958165944634875
exp 95% CrILB	0.0829185477633717	0.0854018789276862
exp 95% CrIUB	0.107013048055469	0.110376559342516
exp ESS	NA	NA
exp Expected results for Likelihood: mean	NA	NA
exp Expected results for Likelihood: SD	NA	NA
exp Expected results for Likelihood: median	NA	NA
exp 95% CrILB	NA	NA
exp 95% CrIUB	NA	NA
exp ESS	NA	NA
exp Expected results for Posterior: mean	0.0952520340671166	0.0956919841329225
exp Expected results for Posterior: SD	0.00443699840518755	0.00476565017698393

Characteristic	Lower Threshold	Upper Threshold
exp Expected results for Posterior: median	0.0951370444537493	0.0956488859440767
exp 95% CrILB	0.0857939236664213	0.0871210359860537
exp 95% CrIUB	0.104244329325227	0.105566113599041
exp ESS	NA	NA

6.2.12 Scenario 12 - Continued study duration with Worst Setting

Scenario 12 describes a binary endpoint for a scenario with a worst case scenario (scenario 4) that continued till the end of the proposed study duration. The scenario characteristics includes huge censoring, huge noise, little events observed, heterogeneous historical and huge prior data conflict.

```
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0.05, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = NA,
  SimStudy_NObsEvt = 400,
  SimStudy_censor_type = 2,
  nStudy = 6,
  tau = 0.15,
  prior_data_conflict = TRUE,
  pdc_hz = c(g1 = 0.05, g2 = 0.1),
  SAF_TOPIC = "Scen12",
  seed = 1701878308
)
```

```
##        STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE   TOT_EXP DOSE FREQ LENGTH  TREAT
## 1_g1 Study#1    1  g1 200    Scen12       193 2145.2002  999  999    999 Scen12
## 2_g1 Study#2    1  g1 200    Scen12       189 2026.7007  999  999    999 Scen12
## 3_g1 Study#3    1  g1 200    Scen12       192 2099.1503  999  999    999 Scen12
## 4_g1 Study#4    1  g1 200    Scen12       193 2200.2265  999  999    999 Scen12
## 5_g1 Study#5    1  g1 200    Scen12       189 2060.4879  999  999    999 Scen12
## 6_g1 Study#6    0  g1 200    Scen12       193 3214.6233  999  999    999 Scen12
## 1_g2 Study#1    1  g2 200    Scen12       196  927.0819  999  999    999 Scen12
## 2_g2 Study#2    1  g2 200    Scen12       193 1097.0120  999  999    999 Scen12
## 3_g2 Study#3    1  g2 200    Scen12       196 1112.5535  999  999    999 Scen12
## 4_g2 Study#4    1  g2 200    Scen12       195 1489.9002  999  999    999 Scen12
## 5_g2 Study#5    1  g2 200    Scen12       198 1575.7302  999  999    999 Scen12
## 6_g2 Study#6    0  g2 200    Scen12       191 1811.5262  999  999    999 Scen12
```

The characteristics and thresholds for the simulation is as in the table below:

```
## [1] "With those values our newly created MAP Prior has been updated:"
```

```
##                                                 csv group
```

```
## Continued Study Duration with Worst Setting Scen12.csv    g1
##                                        analysis saf_topic
## Continued Study Duration with Worst Setting Incidence proportion    Scen12
##                                        seed pool    tau heterog
## Continued Study Duration with Worst Setting 1701878308 TRUE HalfNormal   Large
##                                        ESS rob_weight nta_event nta_npat
## Continued Study Duration with Worst Setting elir       0.5       30      200
```

Characteristic	Lower Threshold	Upper Threshold
log Expected MAP Prior: mean	NA	NA
log Expected MAP Prior: SD	NA	NA
log Expected MAP Prior: median	NA	NA
log 95% CrILB	NA	NA
log 95% CrIUB	NA	NA
log ESS	NA	NA
log Expected robustified MAP Prior: mean	NA	NA
log Expected robustified MAP Prior: SD	NA	NA
log Expected robustified MAP Prior: median	NA	NA
log 95% CrILB	NA	NA
log 95% CrIUB	NA	NA
log ESS	NA	NA
log Expected results for Likelihood: mean	NA	NA
log Expected results for Likelihood: SD	NA	NA
log Expected results for Likelihood: median	NA	NA
log 95% CrILB	NA	NA
log 95% CrIUB	NA	NA
log ESS	NA	NA
log Expected results for Posterior: mean	NA	NA
log Expected results for Posterior: SD	NA	NA
log Expected results for Posterior: median	NA	NA
log 95% CrILB	NA	NA
log 95% CrIUB	NA	NA
log ESS	NA	NA
exp Expected MAP Prior: mean	NA	NA
exp Expected MAP Prior: SD	NA	NA
exp Expected MAP Prior: median	NA	NA
exp 95% CrILB	NA	NA
exp 95% CrIUB	NA	NA
exp ESS	NA	NA
exp Expected robustified MAP Prior: mean	NA	NA
exp Expected robustified MAP Prior: SD	NA	NA
exp Expected robustified MAP Prior: median	NA	NA
exp 95% CrILB	NA	NA
exp 95% CrIUB	NA	NA
exp ESS	NA	NA
exp Expected results for Likelihood: mean	NA	NA
exp Expected results for Likelihood: SD	NA	NA
exp Expected results for Likelihood: median	NA	NA
exp 95% CrILB	NA	NA
exp 95% CrIUB	NA	NA
exp ESS	NA	NA
exp Expected results for Posterior: mean	NA	NA

Characteristic	Lower Threshold	Upper Threshold
exp Expected results for Posterior: SD	NA	NA
exp Expected results for Posterior: median	NA	NA
exp 95% CrILB	NA	NA
exp 95% CrIUB	NA	NA
exp ESS	NA	NA

6.2.13 Scenario 13 - High Dropout & too few people observed

Scenario 13 describes a binary endpoint for a situation with high dropout rate 0f 30%, small noise at a 2% tau, homogeneous historical data, few events being observed and no planned prior data conflict.

```
SimTestData(
  SimStudy_nPat = c(g1 = 200, g2 = 200),
  SimStudy_hz = c(g1 = 0.1, g2 = 0.2),
  SimStudy_dropout = c(rate = 0.3, time = 12),
  SimStudy_accr = 6,
  SimStudy_accr_method = "Uniform",
  SimStudy_surv_method = "Exponential",
  SimStudy_intensity = NA,
  SimStudy_accr_timepoint = NA,
  SimStudy_time_cutoff = 18,
  SimStudy_NObsEvt = 50,
  SimStudy_censor_type = 2,
  nStudy = 6,
  tau = 0.02,
  prior_data_conflict = FALSE,
  pdc_hz = NA,
  SAF_TOPIC = "Scen13",
  seed = 1701879909
)
```

```
##       STUDYID HIST ARM   N SAF_TOPIC N_WITH_AE     TOT_EXP DOSE FREQ LENGTH
## 1_g1 Study#1    1  g1 200    Scen13        11  13.585224  999  999    999
## 2_g1 Study#2    1  g1 200    Scen13        17  58.318673  999  999    999
## 3_g1 Study#3    1  g1 200    Scen13        16  31.614870  999  999    999
## 4_g1 Study#4    1  g1 200    Scen13        15  37.790334  999  999    999
## 5_g1 Study#5    1  g1 200    Scen13        12   2.984491  999  999    999
## 6_g1 Study#6    0  g1 200    Scen13        11 -49.492541  999  999    999
## 1_g2 Study#1    1  g2 200    Scen13        28   3.305205  999  999    999
## 2_g2 Study#2    1  g2 200    Scen13        21  44.281966  999  999    999
## 3_g2 Study#3    1  g2 200    Scen13        27  -9.716870  999  999    999
## 4_g2 Study#4    1  g2 200    Scen13        25   8.577101  999  999    999
## 5_g2 Study#5    1  g2 200    Scen13        30 -29.258983  999  999    999
## 6_g2 Study#6    0  g2 200    Scen13        33 -26.851666  999  999    999
##       TREAT
## 1_g1 Scen13
## 2_g1 Scen13
## 3_g1 Scen13
## 4_g1 Scen13
## 5_g1 Scen13
## 6_g1 Scen13
```

```
## 1_g2 Scen13
## 2_g2 Scen13
## 3_g2 Scen13
## 4_g2 Scen13
## 5_g2 Scen13
## 6_g2 Scen13
```

The characteristics and thresholds for the simulation is as in the table below:

References

[1]   NEUENSCHWANDER, B., CAPKUN-NIGGLI, G., BRANSON, M. and SPIEGELHALTER, D. J. (2010). Summarizing historical information on controls in clinical trials. *Clinical Trials* **7** 5–18.