#18 R Package for Bayesian MCP-Mod Dose Finding Trials

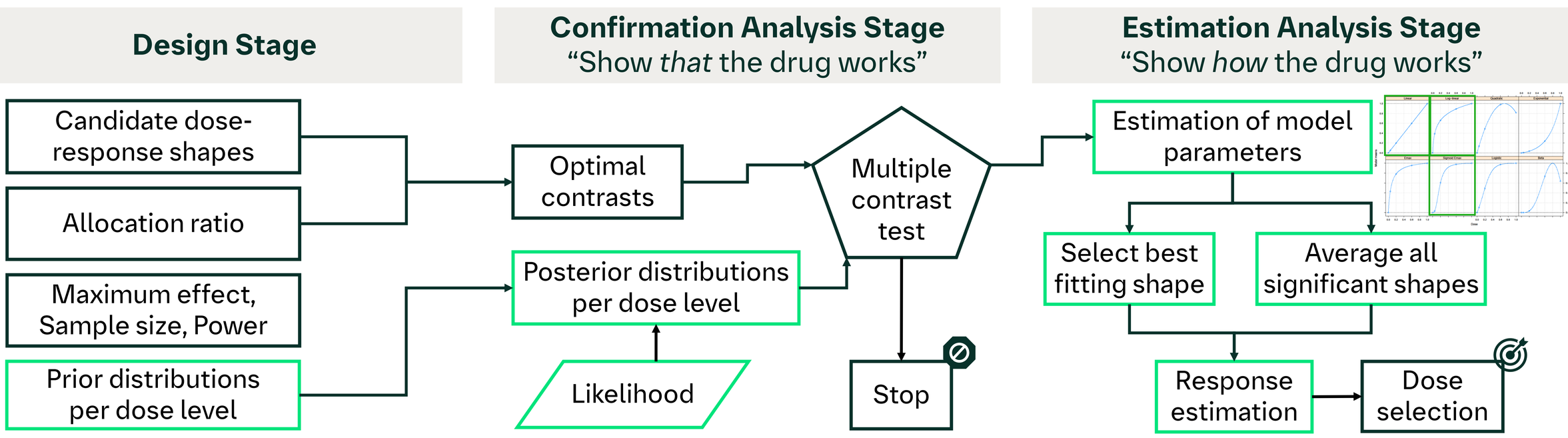
Context

The Multiple Comparison Procedure – Modelling (MCP-Mod) method is well established in dose finding trials.

Bayesian MCP-Mod (1) is an innovative method that improves the traditional MCP-Mod by systematically incorporating historical data, such as previous placebo group data.

This approach replicates classical MCP-Mod results when using vague priors and seamlessly integrates historical data.

Bayesian MCP-Mod in a Nutshell (1, 2)



Outcome

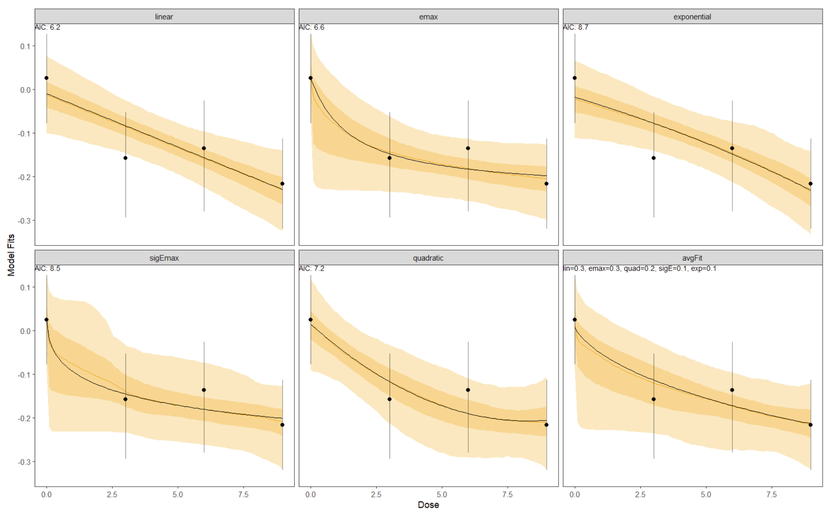
https://CRAN.R-project.org/package=BayesianMCPMod

- **Functions available for Simulating, Analyzing, and Evaluating Bayesian MCP-Mod trials with normally distributed endpoints**
- **Robust mixture prior distributions implemented, e.g., MAP prior (3)**
- **Weighted model averaging approach (4) included for modelling step**
- **Visualization & Bootstrapping implemented for estimated dose-response relationships**
- **Test coverage > 80 % ensures a high code quality**
- **R Package available on CRAN and GitHub**
- **Vignettes available for Analysis Example and Simulation Example**

Trial Analysis

Example Figure

Posterior dose-response relationships for different model shapes



Trial Simulation

```
assessDesign(
  n_patients  = c(80, 60,
                  60, 60,
                  120),
  mods        = mods,
  prior_list  = prior_list,
  sd          = sd_tot,
  n_sim       = 100)
```

```
#> $linear
#> Bayesian Multiple Comparison Procedure
#>   Estimated Success Rate:  0.8
#>   N Simulations:           100
#> Model Significance Frequencies
#>      linear        emax exponential    sigEmax1    sigEmax2
#>        0.76        0.50        0.75        0.65        0.61
#>
#> $emax
#> Bayesian Multiple Comparison Procedure
#>   Estimated Success Rate:  0.84
#>   N Simulations:           100
#> Model Significance Frequencies
#>      linear        emax exponential    sigEmax1    sigEmax2
#>        0.39        0.83        0.34        0.59        0.76
#>
```

Implementation Details

Design

```
DoseFinding::guesst()
DoseFinding::Mods()
getCritProb()
getContr()
RBesT::mixnorm()
performBayesianMCP()
getPosterior()
```

Confirmation

```
getModelFits()
plot()
predict()
getBootstrapSamples()
getBootstrapQuantiles()
```

Estimation

Operating Characteristics

```
DoseFinding::guesst()
DoseFinding::Mods()
getCritProb()
getContr()
RBesT::mixnorm()
assessDesign()
simulateData()
getCritProb()
getContr()
performBayesianMCPMod()
performBayesianMCP()
getModelFits()
```


References

1. Fleischer F, Bossert S, Deng Q, Loley C, Gierse J. Bayesian MCPMod. Pharm Stat. 2022; 21(3):654 – 670.
2. Bretz F, Pinheiro JC, Branson M. Combining multiple comparisons and modeling techniques in dose-response studies. Biometrics. 2005; 61(3): 738-748.
3. Schmidli H, Gsteiger S, Roychoudhury S, O'Hagan A, Spiegelhalter D, Neuenschwander B. Robust meta-analytic-predictive priors in clinical trials with historical control information. Biometrics. 2014 Dec;70(4):1023-32.
4. Pinheiro J, Bornkamp B, Glimm E, Bretz F. Model-based dose finding under model uncertainty using general parametric models. Stat Med 2014 ; 33(10) ; 1646 – 1661

R Packages:

i) DoseFinding: https://cran.r-project.org/package=DoseFinding
ii) RBesT: https://cran.r-project.org/package=RBesT

Abbreviations

- MCP-Mod Multiple Comparison Procedure – Modelling
- MAP Meta-Analytic Predictive

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