01-B-BHM-Simstudy-ORR-report

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# Introduction

## General description

Simulation study to assess the predictive uncertainty in a binary endpoint analyzed with a Bayesian hierarchical model as a function of number of groups and sample size per group.

How perform different design choices (number of groups, size of groups, larger lead group or not)?

What about the analysis model (HN(sigma=1), HN(sigma=0.5), or U(0,5) prior)?

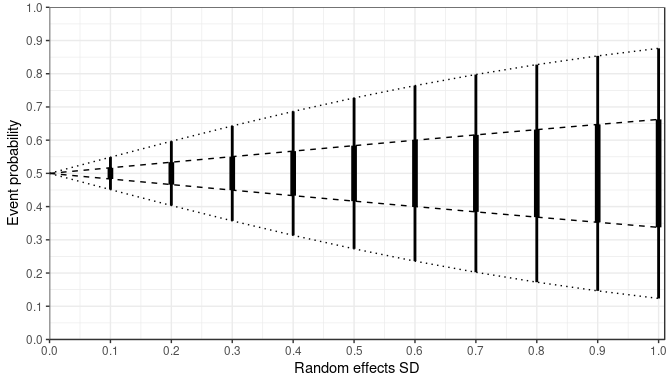
## Defining and interpreting true levels of heterogeneity - how to define a meaningful (analysis) prior for the RE SD?

Assume the true population event rate is and the between-tissue-heterogeneity is . Let be the true rate for tissue and . The random effects model assumes exchangeability on the logit scale, this means

The range of true tissue specific event rates as well as threshold probabilities will depend on .

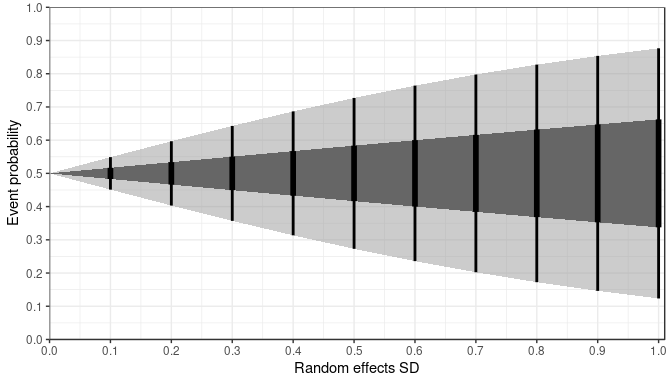
**Figure** 95% and 50% ranges of tissue specific event rates as a function of heterogeneity (random effects SD)

## Warning: Removed 80 rows containing missing values (geom\_path).  
  
## Warning: Removed 80 rows containing missing values (geom\_path).



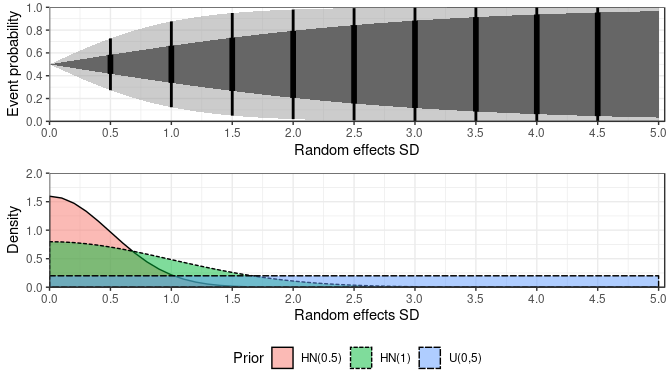
**Figure** idem (alternative version)

## Warning: Removed 40 rows containing missing values (geom\_linerange).  
  
## Warning: Removed 40 rows containing missing values (geom\_linerange).



**Table** 95% and 50% ranges of tissue specific event rates for selected levels of heterogeneity (random effects SD) as well as probability of being below 0.3

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| re.sd | PrIlo | Q1 | Q3 | PrIup | ProbBelow0.3 |
| 0.1 | 0.45 | 0.48 | 0.52 | 0.55 | 0 |
| 0.3 | 0.36 | 0.45 | 0.55 | 0.64 | 0 |
| 0.7 | 0.2 | 0.38 | 0.62 | 0.8 | 0.11 |

**Figure** 50% prediction intervals (dark grey) and 95% prediction intervals (light grey) for true tissue specific event probabilities as a function of RE SD along wtih different prior distributions 

# Simulation settings

## Simulation scenarios

Simulations were run over the full grid of combinations below.

# True rate and heterogeneity  
bin\_grid

## p.pop re.sd  
## 1 0.5 0.1  
## 2 0.5 0.3  
## 3 0.5 0.7

# Sample sizes of lead group and subsequent groups  
size\_grid

## lead.grp lead.grp.size subseq.grp.size  
## 1 yes 20 2  
## 2 yes 20 5  
## 3 yes 20 10  
## 4 no 2 2  
## 5 no 5 5  
## 6 no 10 10  
## 7 no 20 20

# Number of groups  
grp\_grid

## n.grp  
## 1 5  
## 2 7  
## 3 10  
## 4 15  
## 5 20

# Analysis priors (RE SD)  
prior\_grid

## dist  
## 1 U(0,5)  
## 2 HN(0.5)  
## 3 HN(1)

# Resulting full scenario grid  
dim(full\_grid)

## [1] 315 7

head(full\_grid)

## p.pop re.sd lead.grp lead.grp.size subseq.grp.size n.grp dist  
## 1 0.5 0.1 yes 20 2 5 U(0,5)  
## 2 0.5 0.1 yes 20 2 5 HN(0.5)  
## 3 0.5 0.1 yes 20 2 5 HN(1)  
## 4 0.5 0.1 yes 20 2 7 U(0,5)  
## 5 0.5 0.1 yes 20 2 7 HN(0.5)  
## 6 0.5 0.1 yes 20 2 7 HN(1)

tail(full\_grid)

## p.pop re.sd lead.grp lead.grp.size subseq.grp.size n.grp dist  
## 310 0.5 0.7 no 20 20 15 U(0,5)  
## 311 0.5 0.7 no 20 20 15 HN(0.5)  
## 312 0.5 0.7 no 20 20 15 HN(1)  
## 313 0.5 0.7 no 20 20 20 U(0,5)  
## 314 0.5 0.7 no 20 20 20 HN(0.5)  
## 315 0.5 0.7 no 20 20 20 HN(1)

## Global parameters

global\_par

## $n\_sim  
## [1] 500  
##   
## $n\_chains  
## [1] 3  
##   
## $n\_iter  
## [1] 6000  
##   
## $n\_burnin  
## [1] 1000  
##   
## $n\_thin  
## [1] 1  
##   
## $p.threshold  
## [1] 0.3

# Simulation results

Dimension, first and last few lines of results data frame.

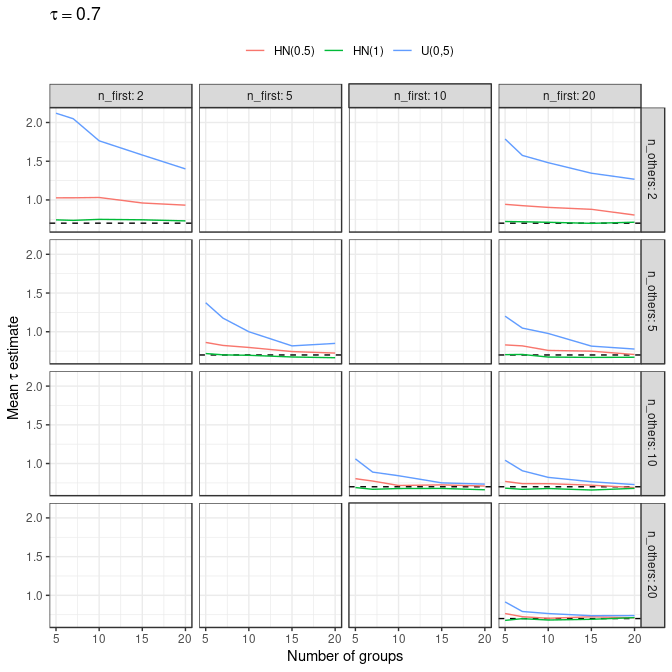
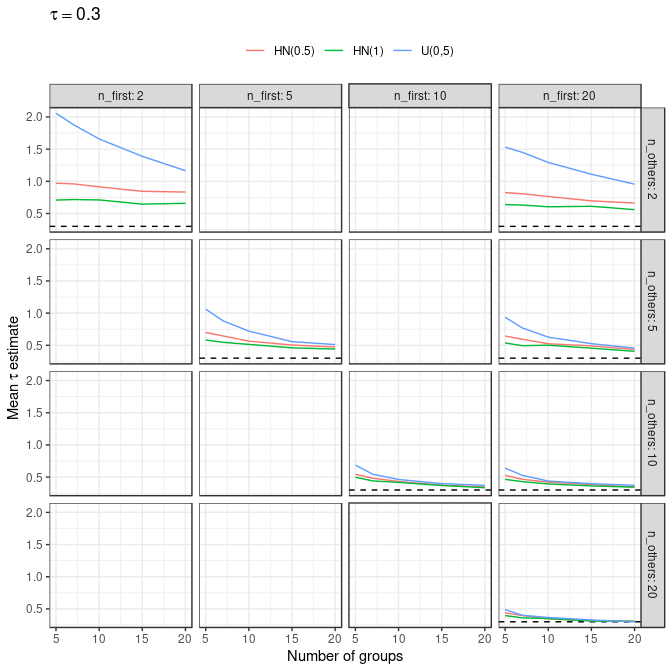
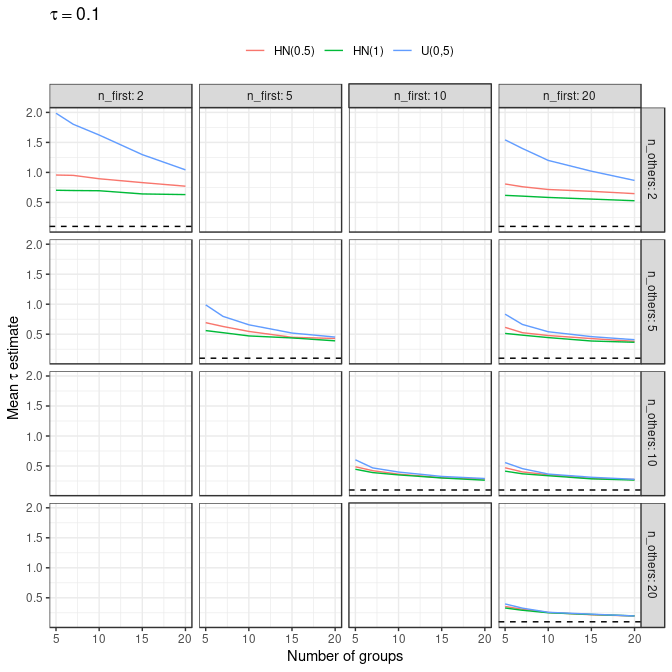
## [1] 28350 15

## scenario node var1 var2 value p.pop re.sd lead.grp lead.grp.size  
## 1 1 p.new 2.5% mean 0.01458807 0.5 0.1 yes 20  
## 2 1 p.new 25% mean 0.28345479 0.5 0.1 yes 20  
## 3 1 p.new 50% mean 0.49803976 0.5 0.1 yes 20  
## 4 1 p.new 75% mean 0.71133409 0.5 0.1 yes 20  
## 5 1 p.new 97.5% mean 0.98294670 0.5 0.1 yes 20  
## 6 1 p.new CrIR mean 0.96835863 0.5 0.1 yes 20  
## subseq.grp.size n.grp dist n.tot n\_first n\_others  
## 1 2 5 U(0,5) 28 20 2  
## 2 2 5 U(0,5) 28 20 2  
## 3 2 5 U(0,5) 28 20 2  
## 4 2 5 U(0,5) 28 20 2  
## 5 2 5 U(0,5) 28 20 2  
## 6 2 5 U(0,5) 28 20 2

## scenario node var1 var2 value p.pop re.sd lead.grp  
## 28345 315 re.sd 25% CIup 0.9340973 0.5 0.7 no  
## 28346 315 re.sd 50% CIup 1.0793763 0.5 0.7 no  
## 28347 315 re.sd 75% CIup 1.2416017 0.5 0.7 no  
## 28348 315 re.sd 97.5% CIup 1.6313821 0.5 0.7 no  
## 28349 315 re.sd CrIR CIup 0.9159291 0.5 0.7 no  
## 28350 315 re.sd IQR CIup 0.3037973 0.5 0.7 no  
## lead.grp.size subseq.grp.size n.grp dist n.tot n\_first n\_others  
## 28345 20 20 20 HN(1) 400 20 20  
## 28346 20 20 20 HN(1) 400 20 20  
## 28347 20 20 20 HN(1) 400 20 20  
## 28348 20 20 20 HN(1) 400 20 20  
## 28349 20 20 20 HN(1) 400 20 20  
## 28350 20 20 20 HN(1) 400 20 20

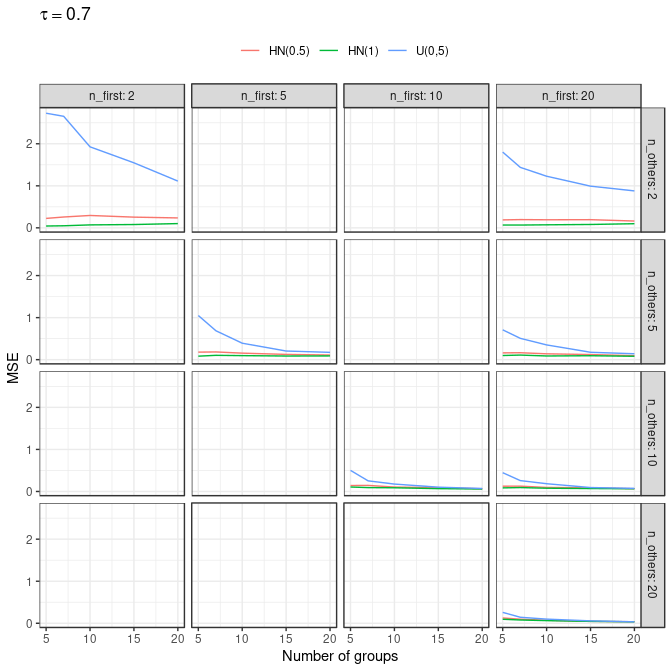
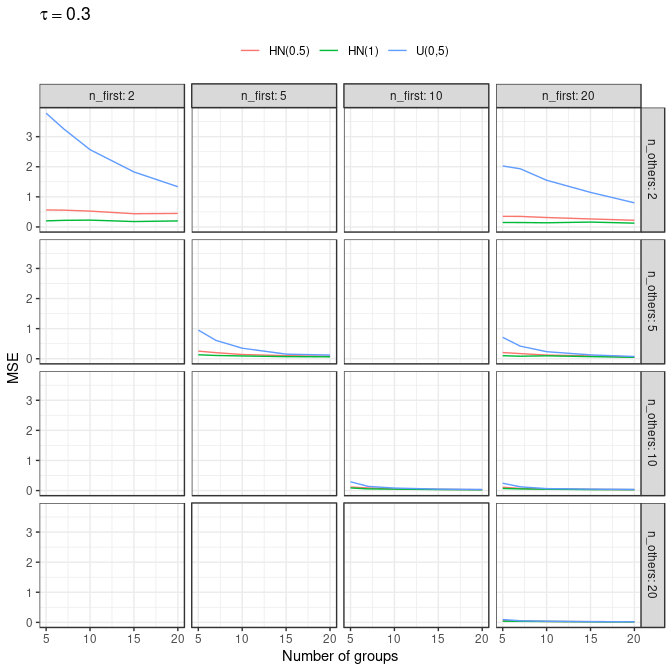
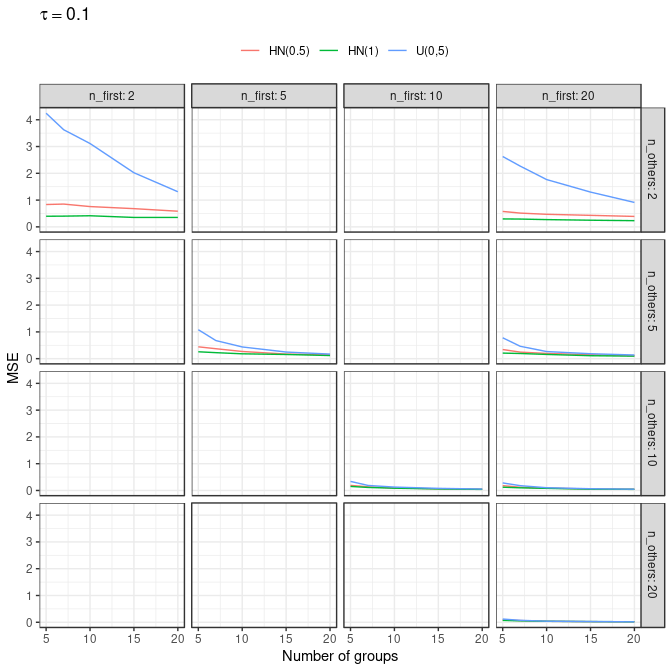
## Estimating between-study-heterogeneity (RE SD)

### Posterior median RE SD ()

**Figure** Posterior median of (mean over 500 simulations) 

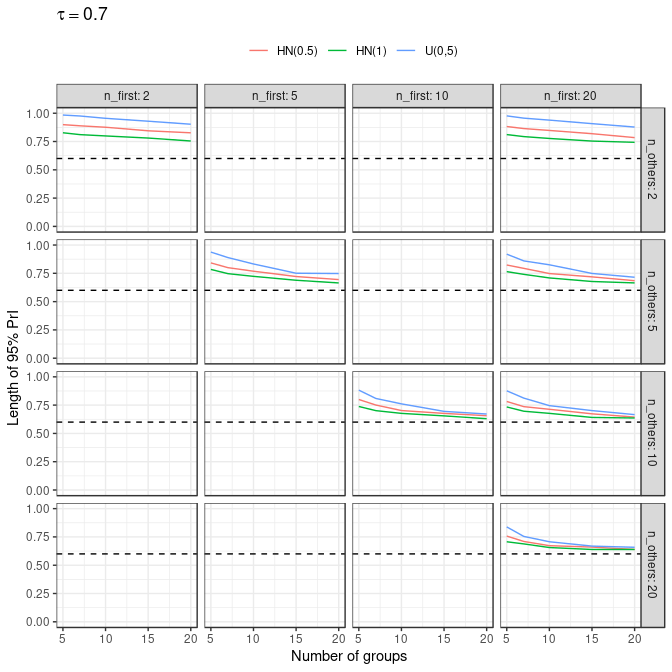
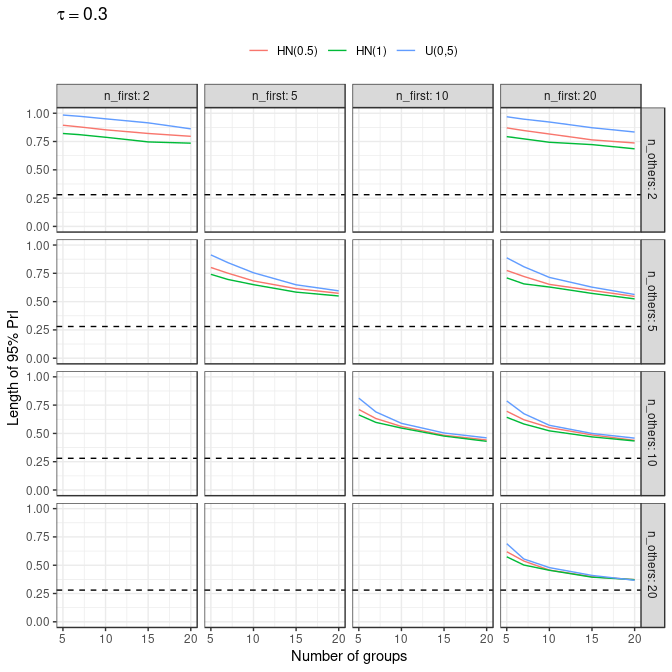
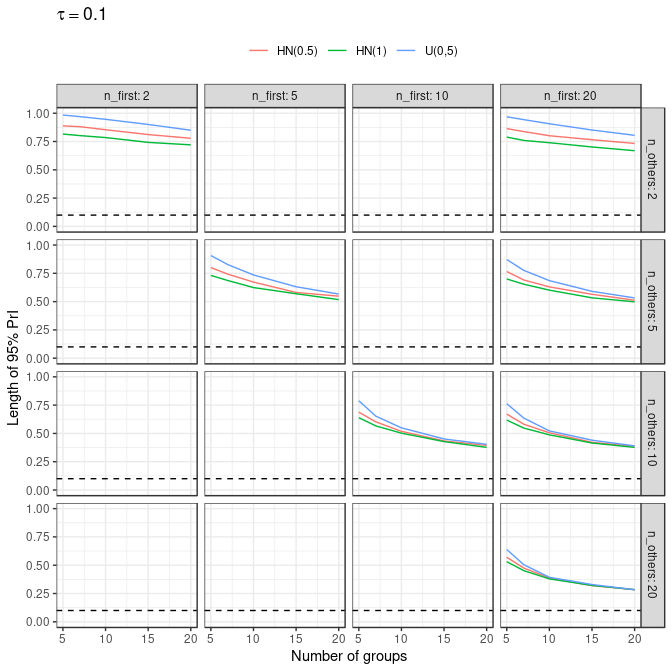
### Mean Squared Error

**Mean Squared Error (MSE)** of the posterior median as an estimator for ,

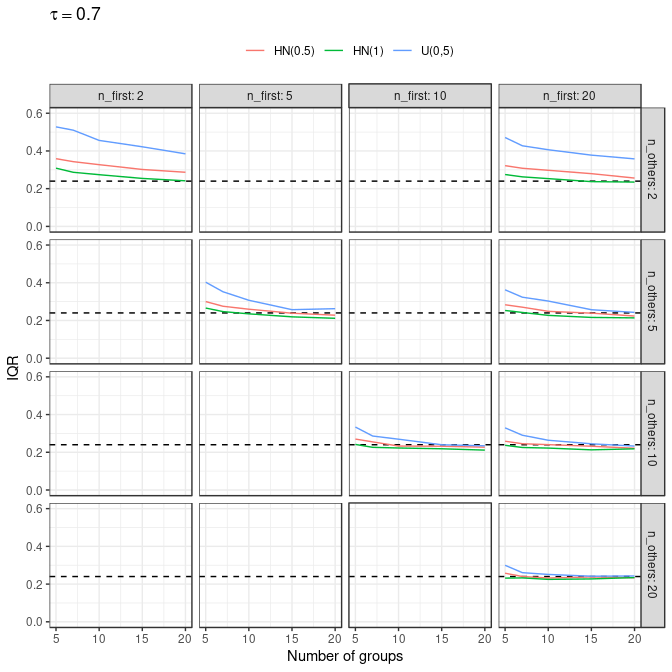
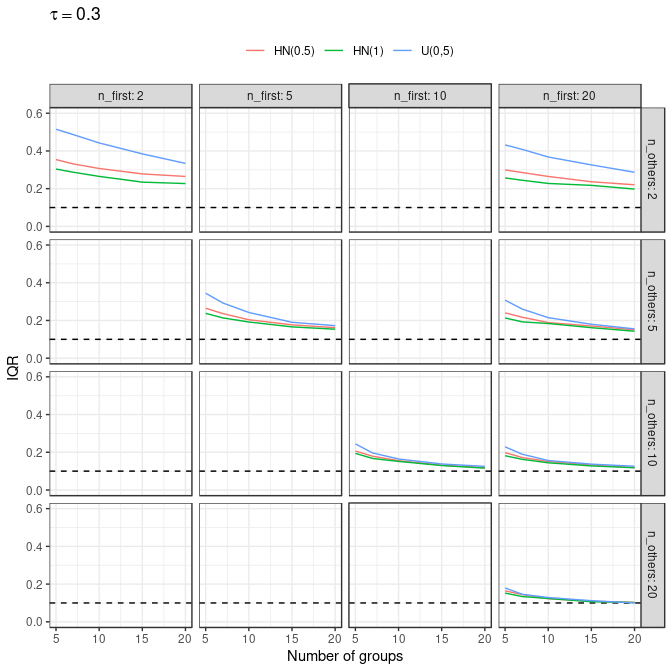
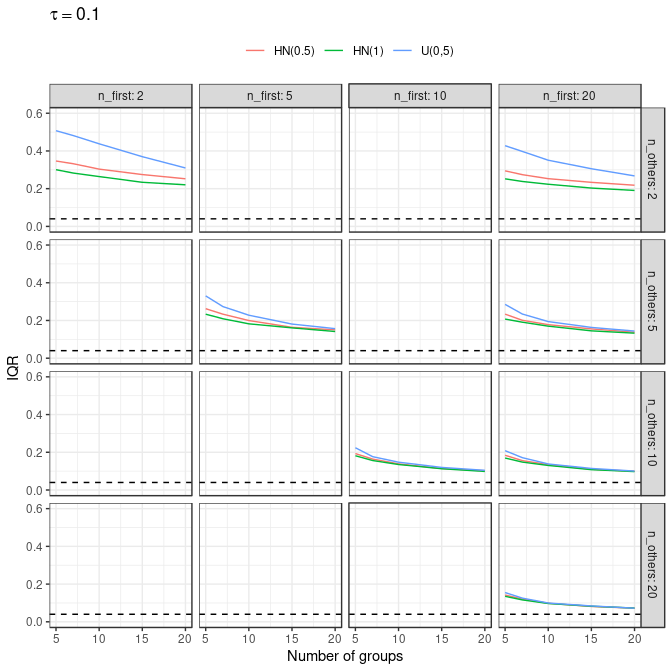
**Figure** MSE of the posterior median RE SD 

## Predictive uncertainty: new tissue response rate

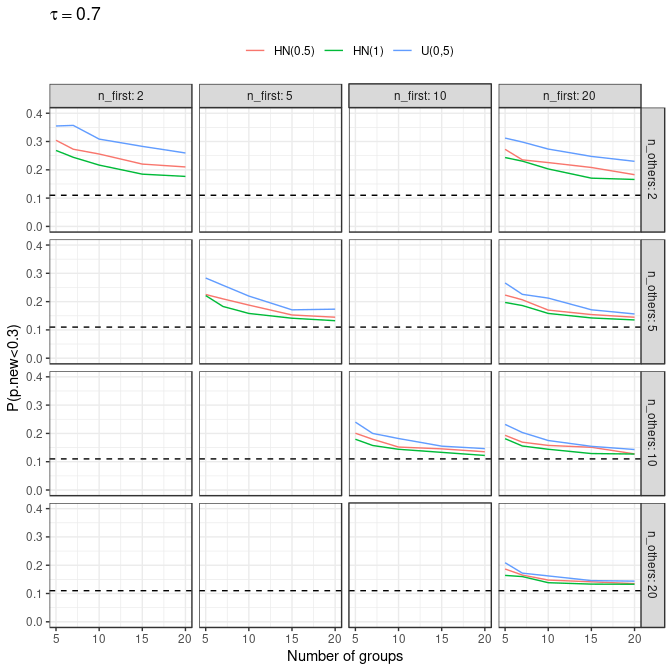
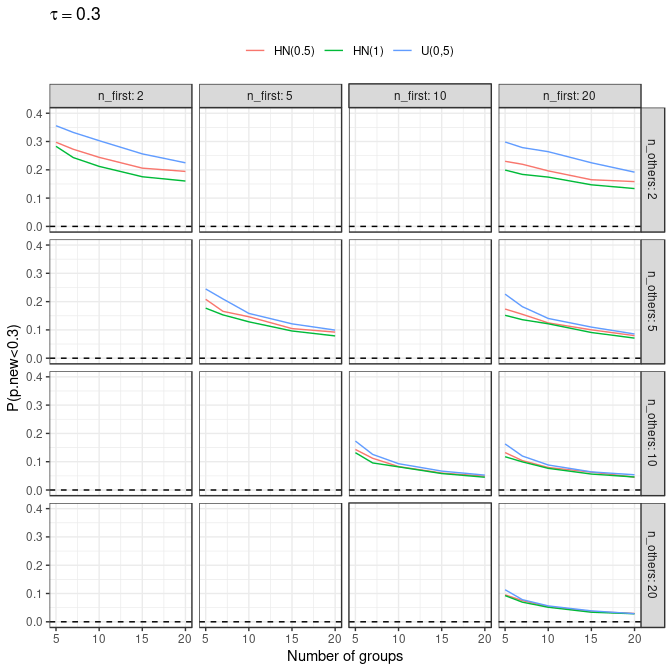
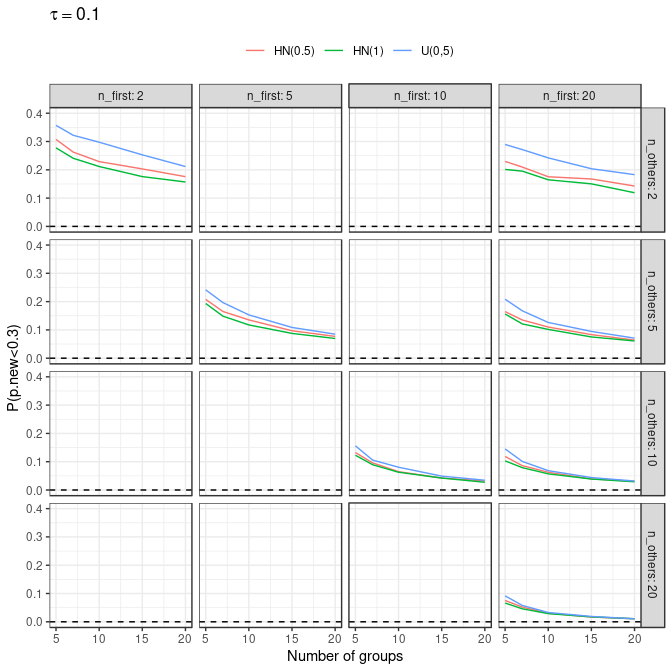
### 95% Prediction interval

**Figure** Length of 95% prediction interval of new group event probability (mean over 500 simulations) 

### Interquartile range

**Figure** Inter-quartile range of prediction interval of new group event probability (mean over 500 simulations) 

### Threshold probabilities

**Figure** Estimated posterior probability of new group event probability being lower than 0.3, P(p.new<0.3) (mean over 500 simulations) 

# Session info

## [1] "/home/bceuser/gsteigs1/GITHUB.COM/punta"

## R version 3.5.3 (2019-03-11)  
## Platform: x86\_64-pc-linux-gnu (64-bit)  
## Running under: Red Hat Enterprise Linux  
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## [5] LC\_MONETARY=en\_US.UTF-8 LC\_MESSAGES=en\_US.UTF-8   
## [7] LC\_PAPER=en\_US.UTF-8 LC\_NAME=C   
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## [11] LC\_MEASUREMENT=en\_US.UTF-8 LC\_IDENTIFICATION=C   
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##   
## other attached packages:  
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##   
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