UNIVERSITY OF AMSTERDAM

Empirical Prior Distributions for Bayesian Meta-Analyses of Binary and Time to Event Outcomes

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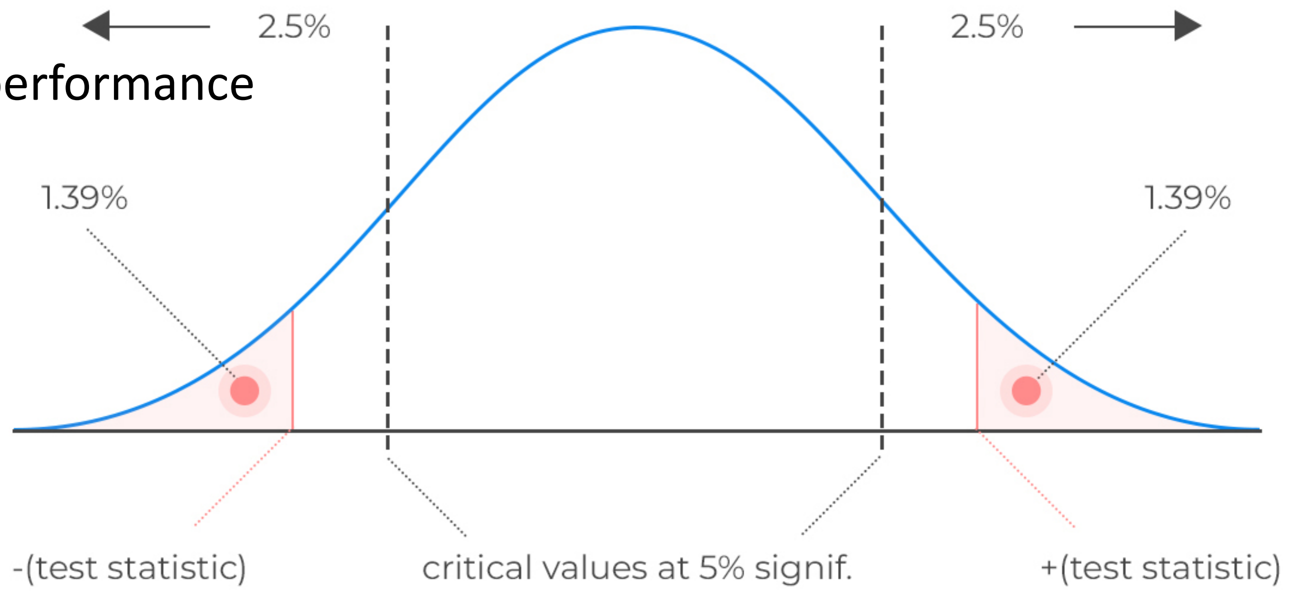
Outline

- Bayesian hypothesis testing
- Bayesian model-averaged meta-analysis
- Empirical prior distributions
- Example

Bayesian Hypothesis Testing

- Requires specification of both H_0 and H_1
  - vs. NHST requiring only H_0
- Bayes factors
  - Compares models via prior predictive performance



Bayesian Hypothesis Testing

$$p(\text{data} \mid \mathcal{H}_0) = \int p(\text{data} \mid \theta_0, \mathcal{H}_0)\, p(\theta_0 \mid \mathcal{H}_0)\, \mathrm{d}\theta_0$$

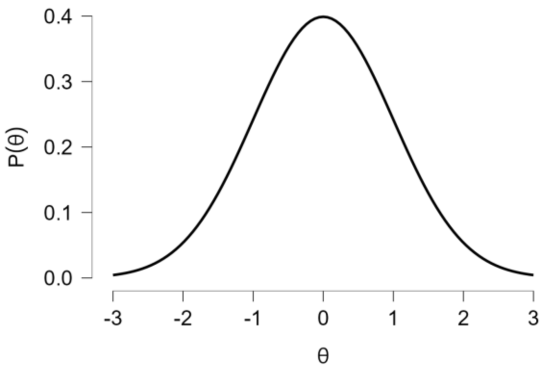
$$p(\text{data} \mid \mathcal{H}_1) = \int p(\text{data} \mid \theta_1, \mathcal{H}_1)\, p(\theta_1 \mid \mathcal{H}_1)\, \mathrm{d}\theta_1$$

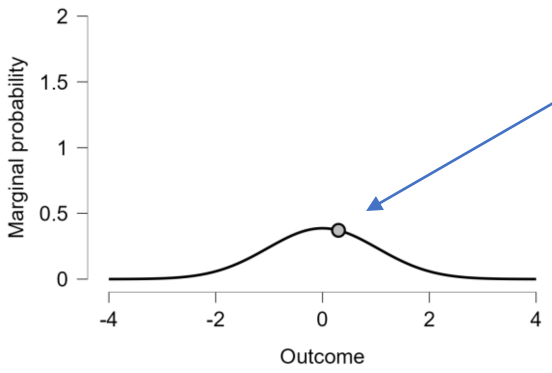
Alternative hypothesis vs. null hypothesis

Prior distribution

Prior predictive distribution

H_1 :

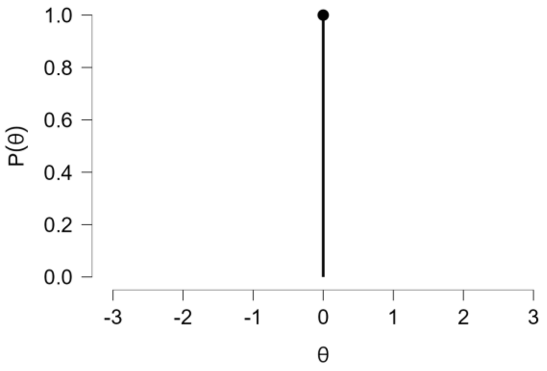


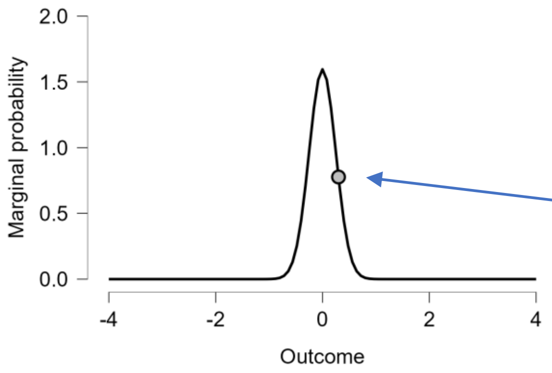


Probability of the data under H_1

$$\mathrm{BF}_{10} = \frac{p(\text{data} \mid \mathcal{H}_1)}{p(\text{data} \mid \mathcal{H}_0)}$$

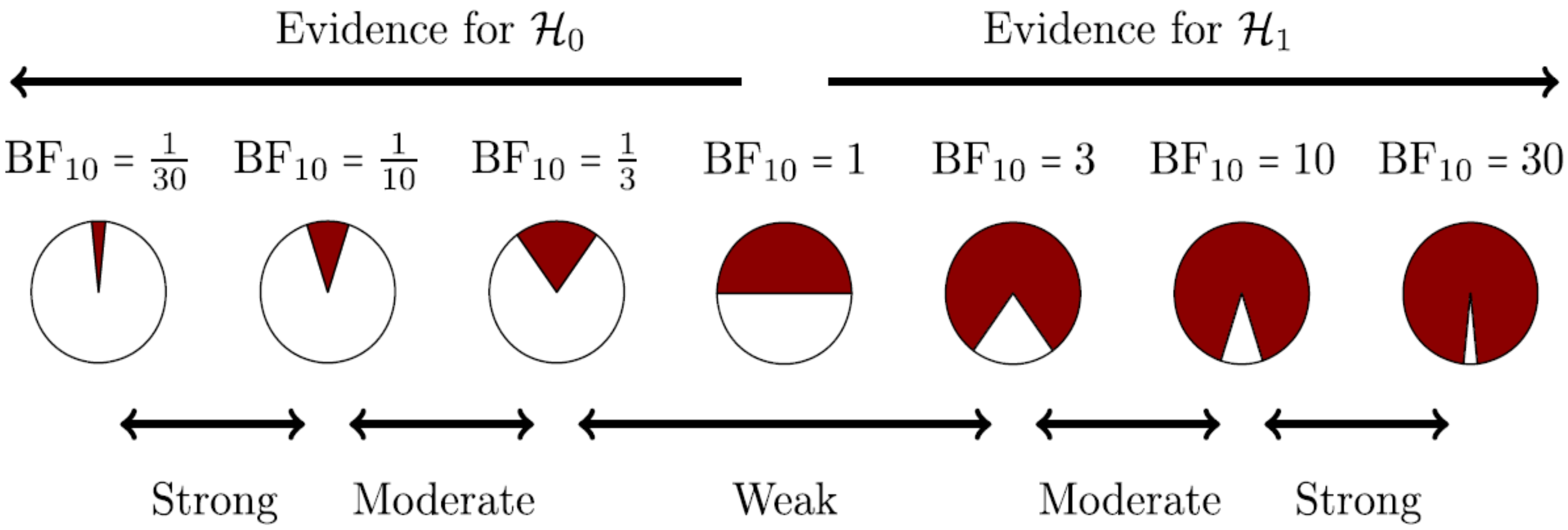
H_0 :





Probability of the data under H_0

Bayesian Hypothesis Testing



$$\mathrm{BF}_{10} = \frac{p(\text{data} \mid \mathcal{H}_1)}{p(\text{data} \mid \mathcal{H}_0)}$$

Bayesian Meta-Analyses (Normal-Normal Model)

Population mean effect μ

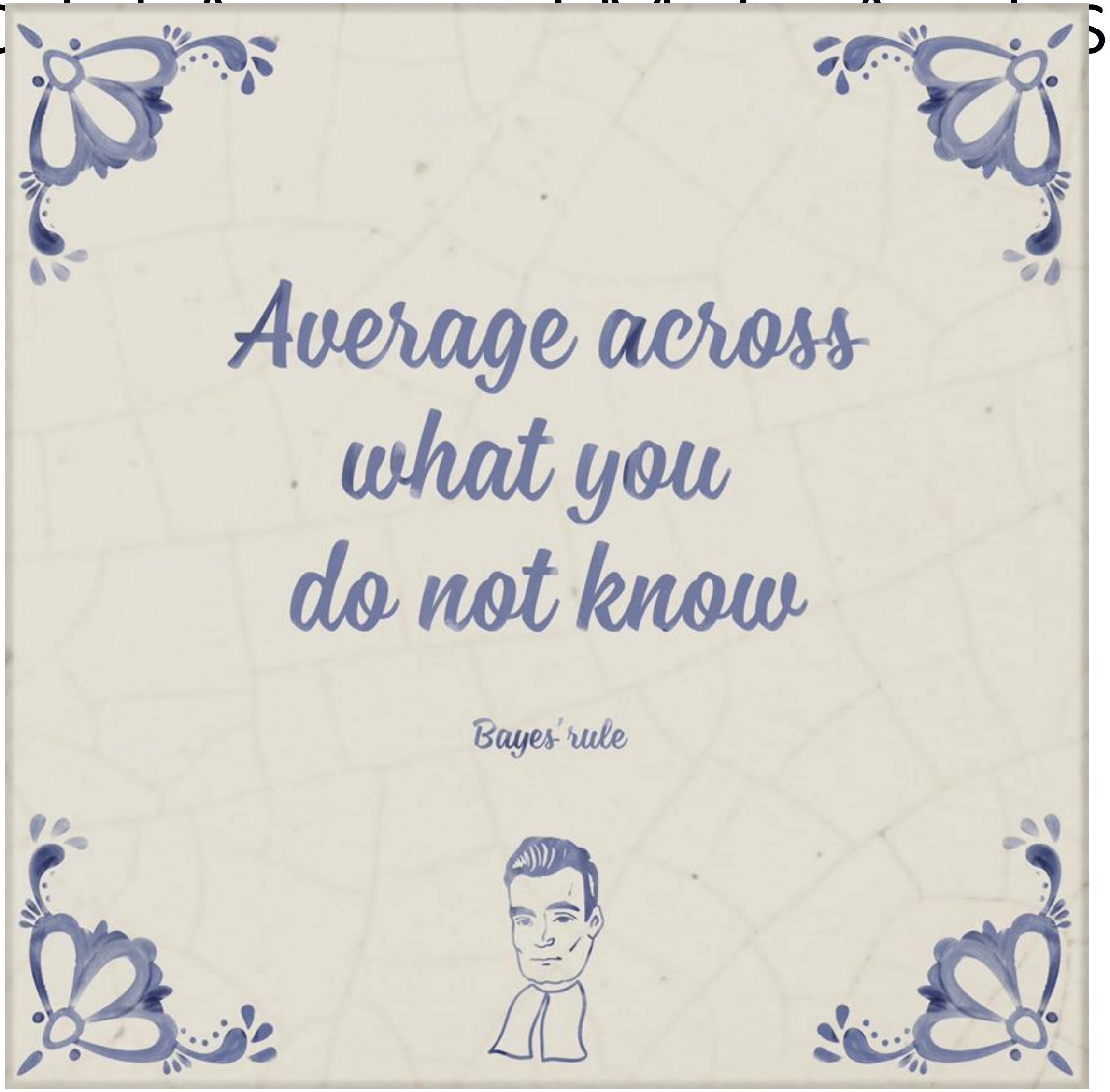
Between-study heterogeneity τ

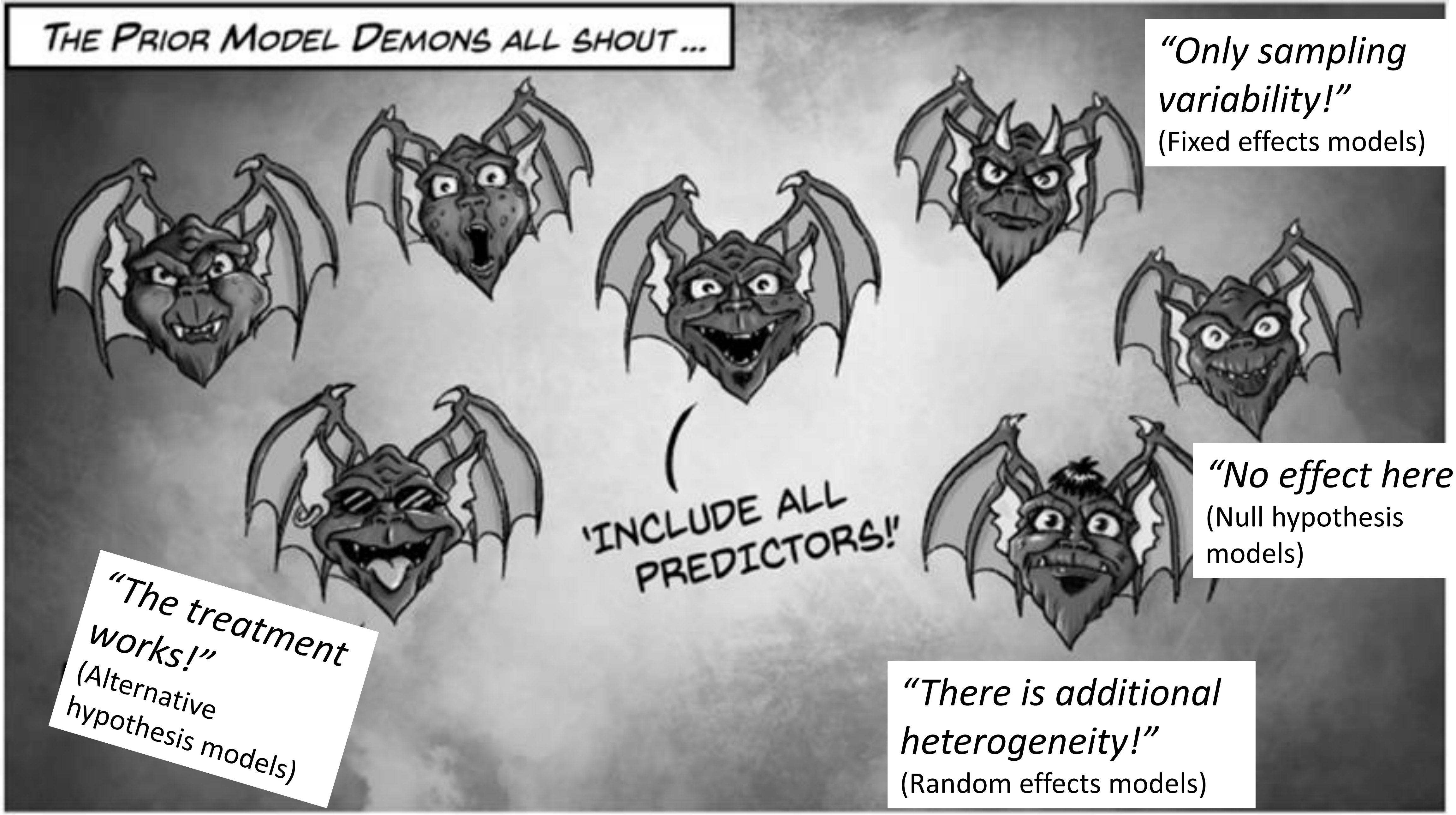
$$\mu \sim f()$$
$$\tau \sim g()$$
$$\mathrm{y}_i \sim \mathrm{Normal}(\mu, \mathrm{se}_i^2 + \tau^2)$$

Four possible models:

1. the fixed-effect null hypothesis $\mathcal{H}_0^f : \mu = 0 \ , \tau = 0$
2. the fixed-effect alternative hypothesis $\mathcal{H}_1^f : \mu \sim f() \ , \tau = 0$
3. the random-effects null hypothesis $\mathcal{H}_0^r : \mu = 0, \tau \sim g()$
4. the random-effects alternative hypothesis $\mathcal{H}_1^r : \mu \sim f() \ , \tau \sim g()$

Bayesian Mo … sis





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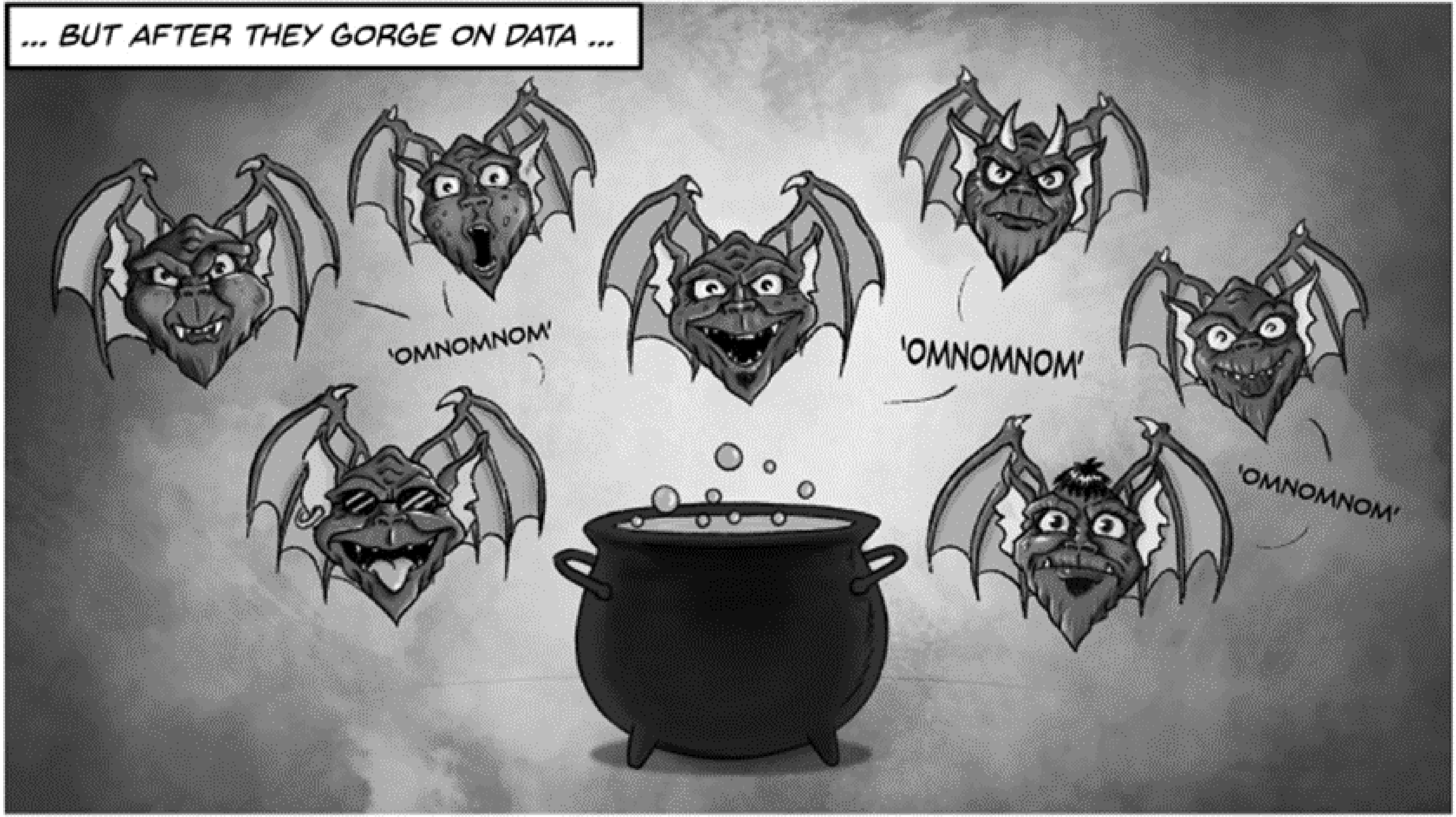

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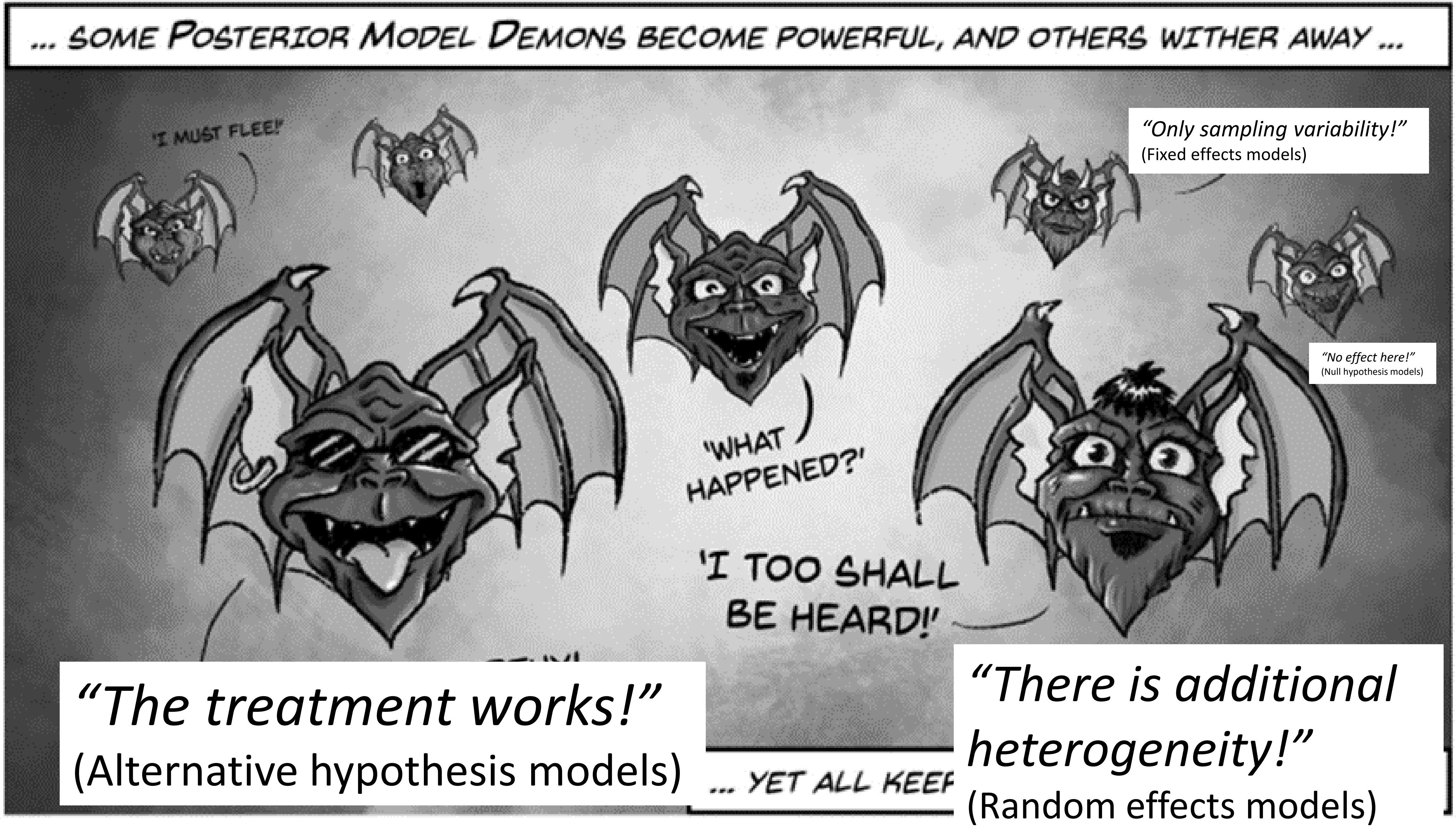

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Bayesian Model-Averaged Meta-Analysis

$$\mathrm{BF}_{10} = \frac{p(\text{data} \mid \mathcal{H}_1)}{p(\text{data} \mid \mathcal{H}_0)}$$

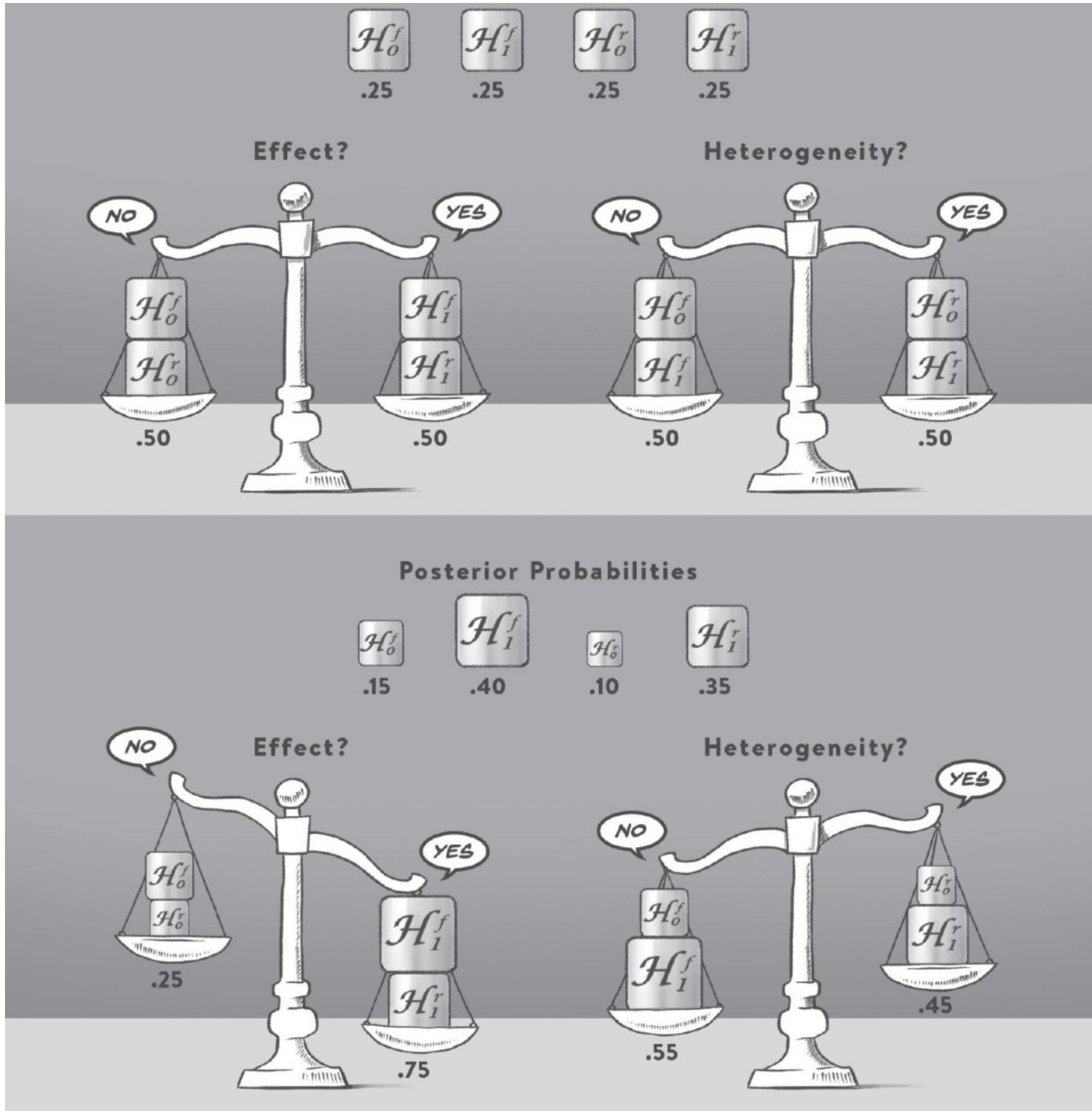
$$\mathrm{BF}_{10} = \underbrace{\frac{p(\mathcal{H}_1 \mid \text{data})}{p(\mathcal{H}_0 \mid \text{data})}}_{\text{Posterior odds}} \Big/ \underbrace{\frac{p(\mathcal{H}_1)}{p(\mathcal{H}_0)}}_{\text{Prior odds}}$$

Bayesian Model-Averaged Meta-Analysis

Inclusion Bayes factors:

$$\underbrace{\mathrm{BF}_{10}}_{\text{Inclusion BF for effect}} = \underbrace{\frac{p(\mathcal{H}_1^{\,f} \mid \text{data}) + p(\mathcal{H}_1^{\,r} \mid \text{data})}{p(\mathcal{H}_0^{\,f} \mid \text{data}) + p(\mathcal{H}_0^{\,r} \mid \text{data})}}_{\text{Posterior inclusion odds for effect}} \Big/ \underbrace{\frac{p(\mathcal{H}_1^{\,f}) + p(\mathcal{H}_1^{\,r})}{p(\mathcal{H}_0^{\,f}) + p(\mathcal{H}_0^{\,r})}}_{\text{Prior inclusion odds for effect}}$$

$$\underbrace{\mathrm{BF}_{rf}}_{\text{Inclusion BF for heterogeneity}} = \underbrace{\frac{p(\mathcal{H}_0^{\,r} \mid \text{data}) + p(\mathcal{H}_1^{\,r} \mid \text{data})}{p(\mathcal{H}_0^{\,f} \mid \text{data}) + p(\mathcal{H}_1^{\,f} \mid \text{data})}}_{\text{Posterior inclusion odds for heterogeneity}} \Big/ \underbrace{\frac{p(\mathcal{H}_0^{\,r}) + p(\mathcal{H}_1^{\,r})}{p(\mathcal{H}_0^{\,f}) + p(\mathcal{H}_1^{\,f})}}_{\text{Prior inclusion odds for heterogeneity}}$$



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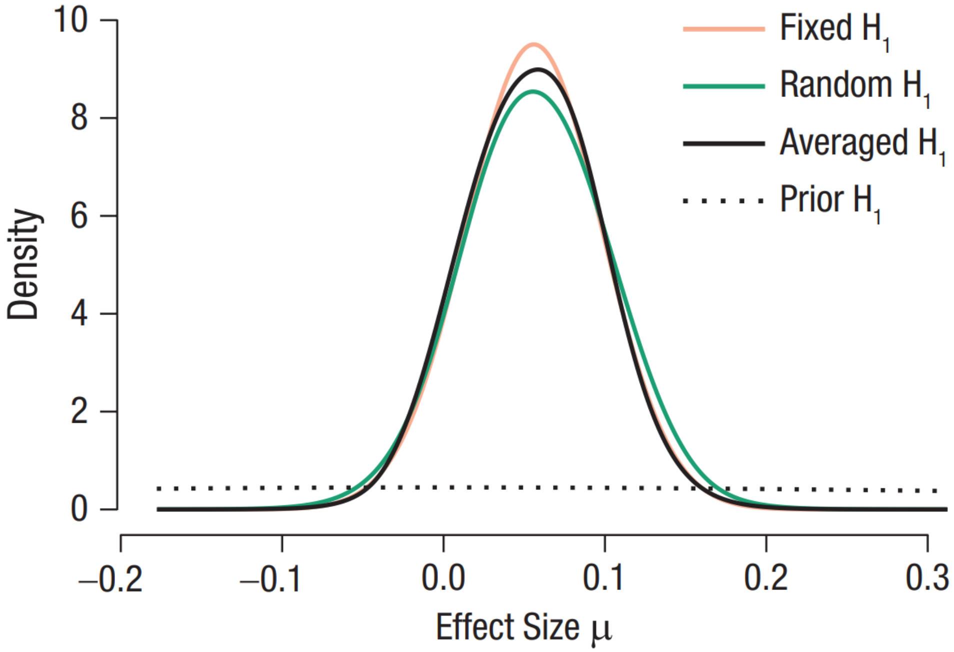
Bayesian Model-Averaged Meta-Analysis

Model-averaged posterior distributions:

$$\underbrace{p(\mu \mid \text{data}, \mathcal{H}_1)}_{\substack{\text{Model-averaged}\\ \text{posterior distribution}\\ \text{for effect}}} \propto \underbrace{p(\mu \mid \mathcal{H}_1^f, \text{data})}_{\substack{\text{Posterior prob.}\\ \text{of } \mathcal{H}_1^f}} \times \underbrace{p(\mathcal{H}_1^f \mid \text{data})}_{\substack{\text{Posterior distr.}\\ \text{of the effect}\\ \text{under } \mathcal{H}_1^f}} + \underbrace{p(\mu \mid \mathcal{H}_1^r, \text{data})}_{\substack{\text{Posterior prob.}\\ \text{of } \mathcal{H}_1^r}} \times \underbrace{p(\mathcal{H}_1^r \mid \text{data})}_{\substack{\text{Posterior distr.}\\ \text{of the effect}\\ \text{under } \mathcal{H}_1^r}}$$

$$\underbrace{p(\tau \mid \text{data}, \mathcal{H}^r)}_{\substack{\text{Model-averaged}\\ \text{posterior distribution}\\ \text{for heterogeneity}}} \propto \underbrace{p(\mu \mid \mathcal{H}_0^r, \text{data})}_{\substack{\text{Posterior prob.}\\ \text{of } \mathcal{H}_0^r}} \times \underbrace{p(\mathcal{H}_0^r \mid \text{data})}_{\substack{\text{Posterior distr.}\\ \text{of heterogeneity}\\ \text{under } \mathcal{H}_0^r}} + \underbrace{p(\mu \mid \mathcal{H}_1^r, \text{data})}_{\substack{\text{Posterior prob.}\\ \text{of } \mathcal{H}_1^r}} \times \underbrace{p(\mathcal{H}_1^r \mid \text{data})}_{\substack{\text{Posterior distr.}\\ \text{of heterogeneity}\\ \text{under } \mathcal{H}_1^r}}$$



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Binomial-Normal Model

Population mean effect μ

Between-study heterogeneity τ

Random-effects γ

Baseline probability β

	Events	Non-Events	N
Group 1	a	b	n_1
Group 2	c	d	n_2

$$
\begin{aligned}
a_i &\sim \mathrm{Binomial}(\pi_{1,i}, n_{1,i}),\\
c_i &\sim \mathrm{Binomial}(\pi_{2,i}, n_{2,i}),\\
\mathrm{logit}(\pi_{1,i}) &= \beta_i + \gamma_i/2,\\
\mathrm{logit}(\pi_{2,i}) &= \beta_i - \gamma_i/2,\\
\gamma_i &\sim \mathrm{Normal}(\mu, \tau),
\end{aligned}
$$

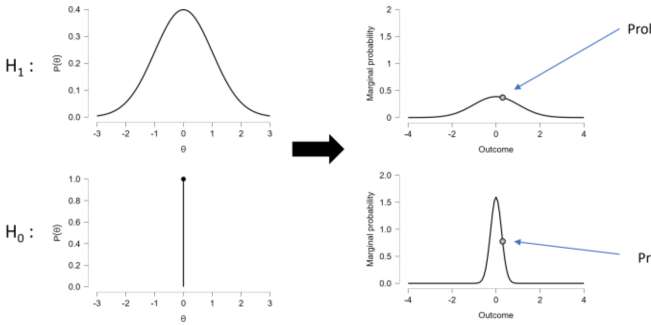
Prior Distributions

Bayesian Hypothesis Testing

Alternative hypothesis vs. null hypothesis

$$p(\text{data} \mid \mathcal{H}_0) = \int p(\text{data} \mid \theta_0, \mathcal{H}_0)\, p(\theta_0 \mid \mathcal{H}_0)\, \mathrm{d}\theta_0$$

$$p(\text{data} \mid \mathcal{H}_1) = \int p(\text{data} \mid \theta_1, \mathcal{H}_1)\, p(\theta_1 \mid \mathcal{H}_1)\, \mathrm{d}\theta_1$$



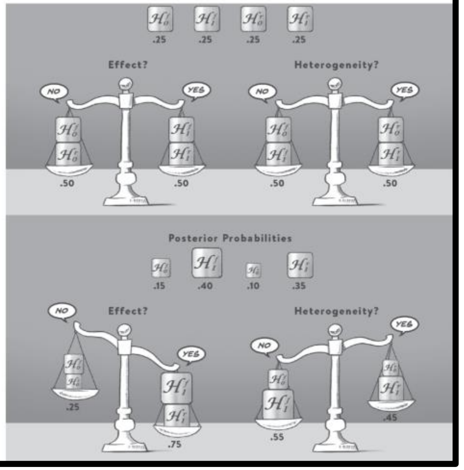
$$\mathrm{BF}_{10} = \frac{p(\text{data} \mid \mathcal{H}_1)}{p(\text{data} \mid \mathcal{H}_0)}$$

Bayesian Model-Averaged Meta-Analysis

Inclusion Bayes factors:

$$\underbrace{\mathrm{BF}_{10}}_{\substack{\text{Inclusion BF}\\ \text{for effect}}} = \underbrace{\frac{p(\mathcal{H}_1^f \mid \text{data}) + p(\mathcal{H}_1^r \mid \text{data})}{p(\mathcal{H}_0^f \mid \text{data}) + p(\mathcal{H}_0^r \mid \text{data})}}_{\substack{\text{Posterior inclusion odds}\\ \text{for effect}}} \Big/ \underbrace{\frac{p(\mathcal{H}_1^f) + p(\mathcal{H}_1^r)}{p(\mathcal{H}_0^f) + p(\mathcal{H}_0^r)}}_{\substack{\text{Prior inclusion odds}\\ \text{for effect}}}$$

$$\underbrace{\mathrm{BF}_{rf}}_{\substack{\text{Inclusion BF}\\ \text{for heterogeneity}}} = \underbrace{\frac{p(\mathcal{H}_0^r \mid \text{data}) + p(\mathcal{H}_1^r \mid \text{data})}{p(\mathcal{H}_0^f \mid \text{data}) + p(\mathcal{H}_1^f \mid \text{data})}}_{\substack{\text{Posterior inclusion odds}\\ \text{for heterogeneity}}} \Big/ \underbrace{\frac{p(\mathcal{H}_0^r) + p(\mathcal{H}_1^r)}{p(\mathcal{H}_0^f) + p(\mathcal{H}_1^f)}}_{\substack{\text{Prior inclusion odds}\\ \text{for heterogeneity}}}$$



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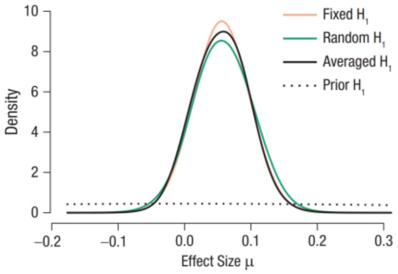
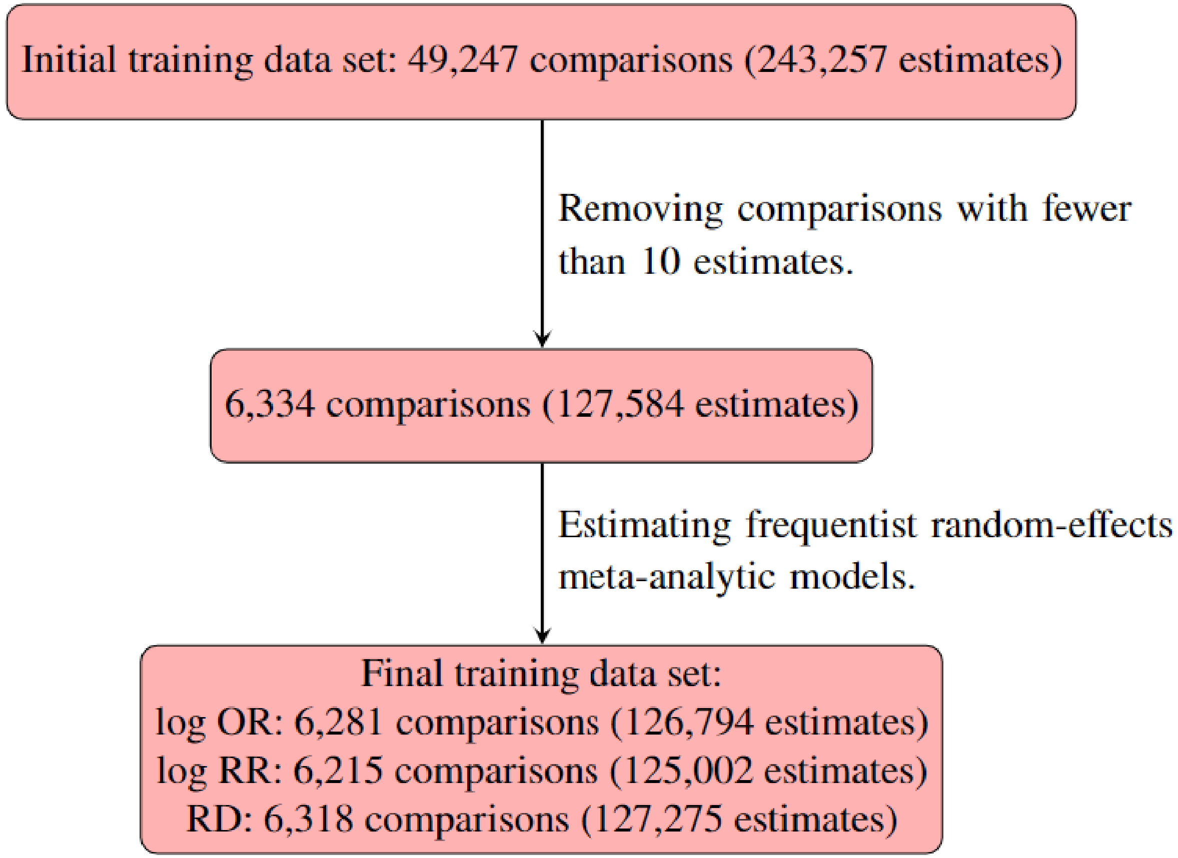
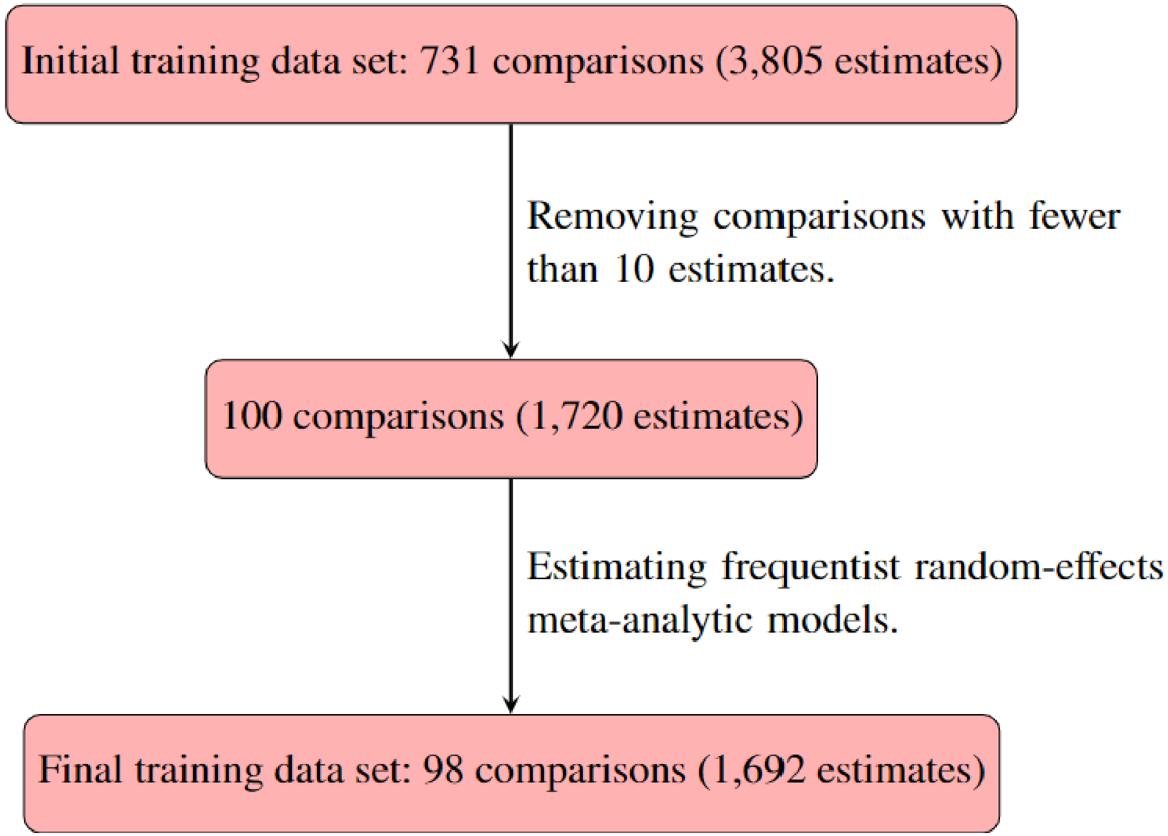
$$\underbrace{p(\tau \mid \text{data}, \mathcal{H}^r)}_{\substack{\text{Model-averaged}\\ \text{posterior distribution}\\ \text{for heterogeneity}}} \propto \underbrace{p(\mu \mid \mathcal{H}_0^r, \text{data})}_{\substack{\text{Posterior prob.}\\ \text{of } \mathcal{H}_0^r}} \times \underbrace{p(\mathcal{H}_0^r \mid \text{data})}_{\substack{\text{Posterior distr.}\\ \text{of heterogeneity}\\ \text{under } \mathcal{H}_0^r}} + \underbrace{p(\mu \mid \mathcal{H}_1^r, \text{data})}_{\substack{\text{Posterior prob.}\\ \text{of } \mathcal{H}_1^r}} \times \underbrace{p(\mathcal{H}_1^r \mid \text{data})}_{\substack{\text{Posterior distr.}\\ \text{of heterogeneity}\\ \text{under } \mathcal{H}_1^r}}$$



Training Data Set

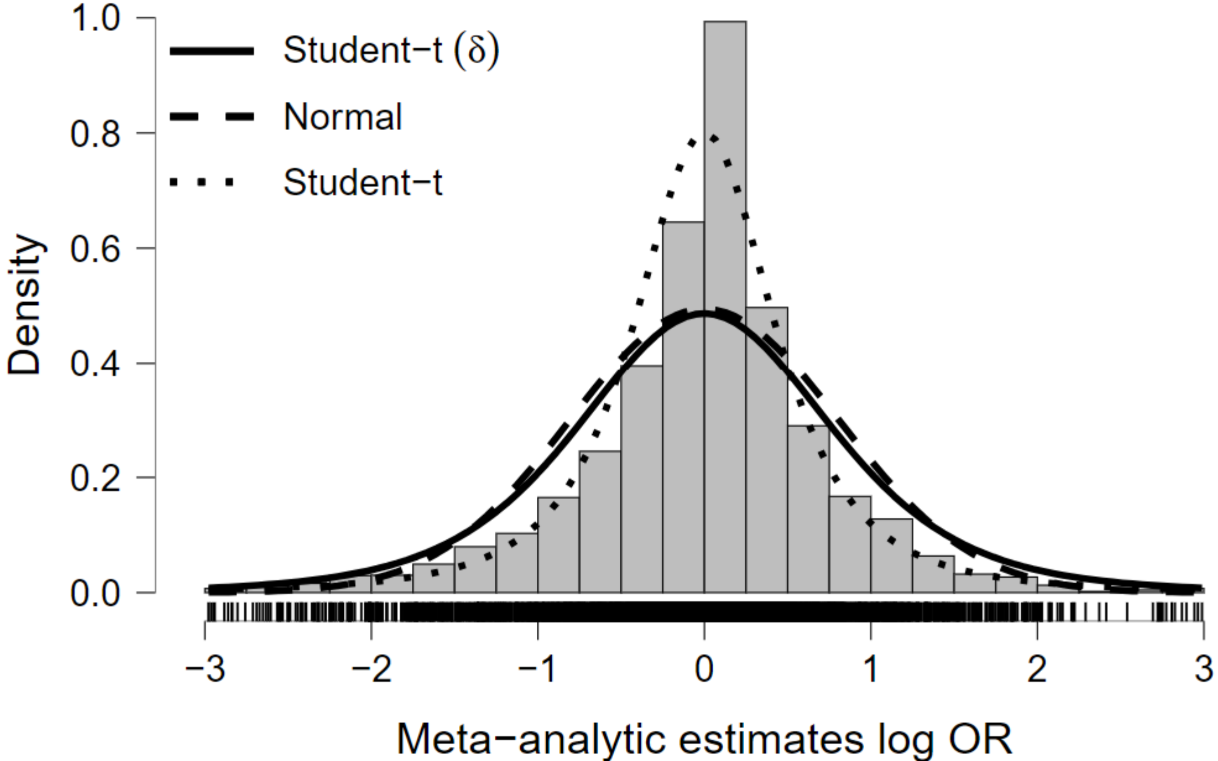


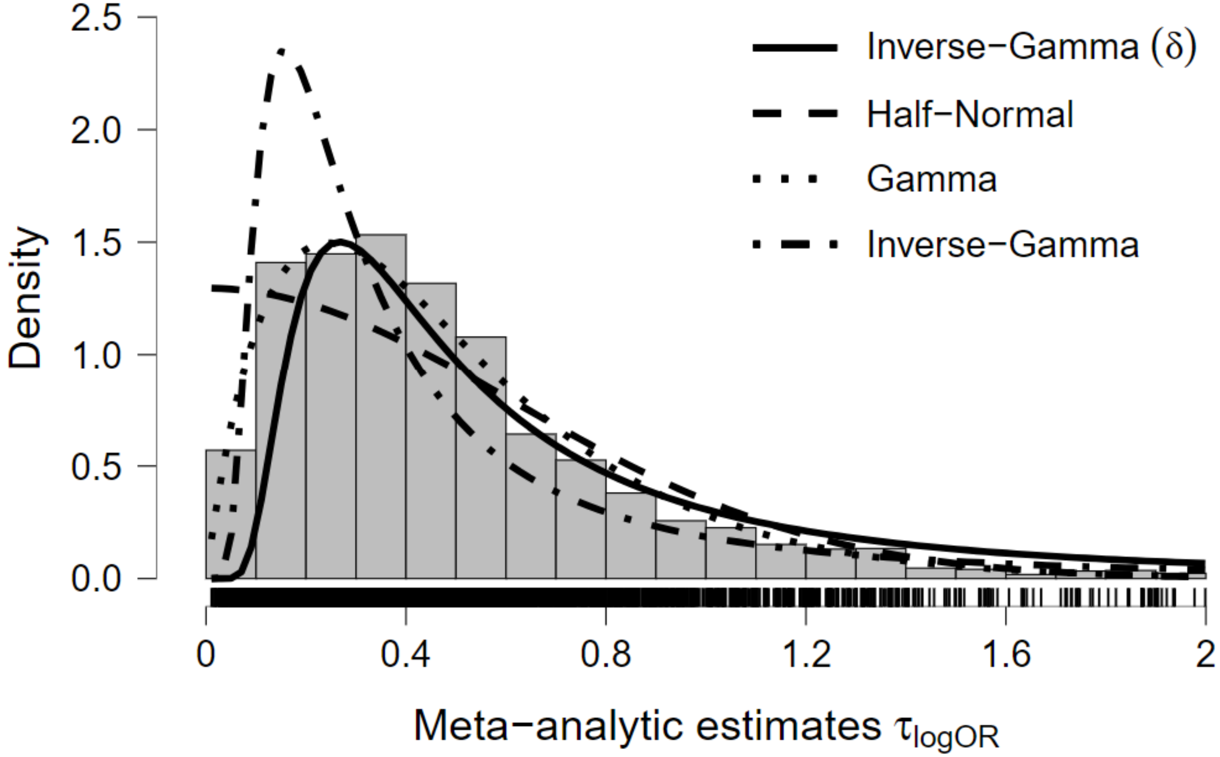


Prior Distributions for log OR

Binary outcomes as log OR

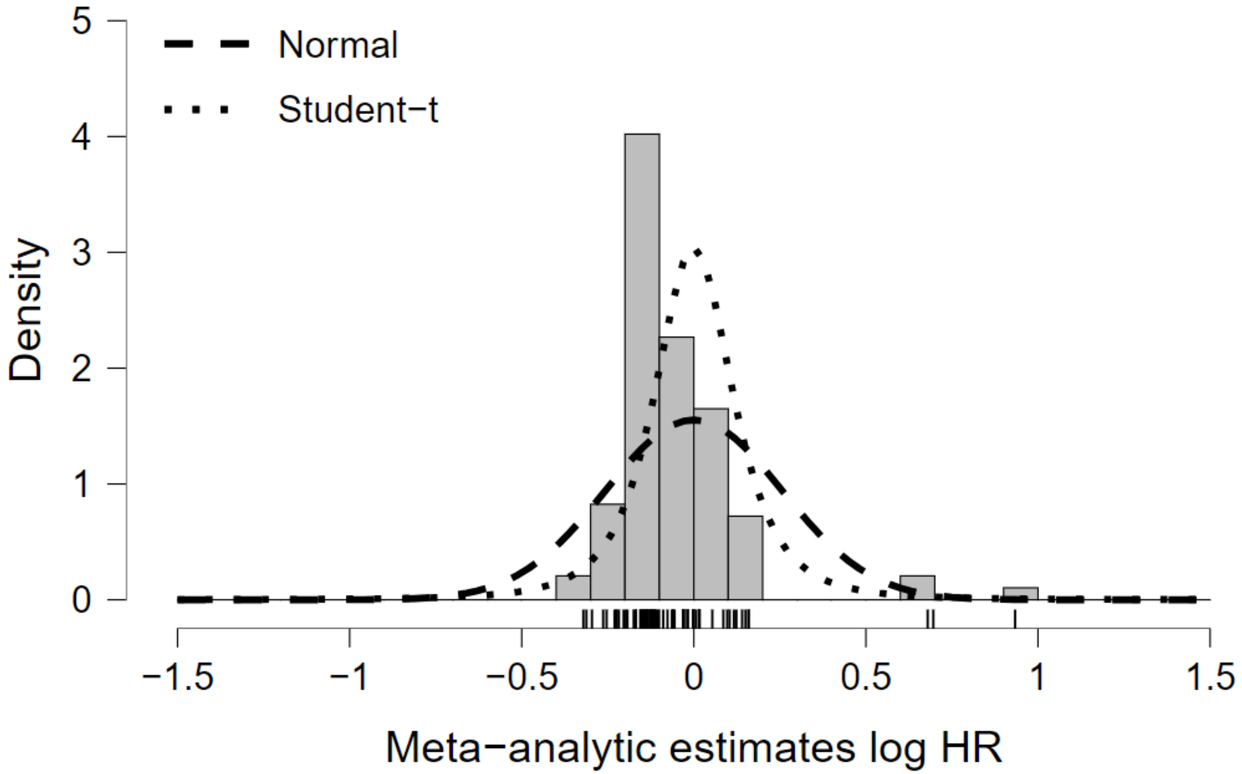
$\mu \sim \text{Student-t}(0, 0.78, 5)$	$\tau \sim \text{Inv-Gamma}(1.71, 0.73)$
$\mu \sim \text{Normal}(0, 0.81)$	$\tau \sim \text{Normal}_{+}(0, 0.62)$
$\mu \sim \text{Student-t}(0, 0.45, 2.38)$	$\tau \sim \text{Inv-Gamma}(1.53, 0.40)$
	$\tau \sim \text{Gamma}(1.99, 0.25)$

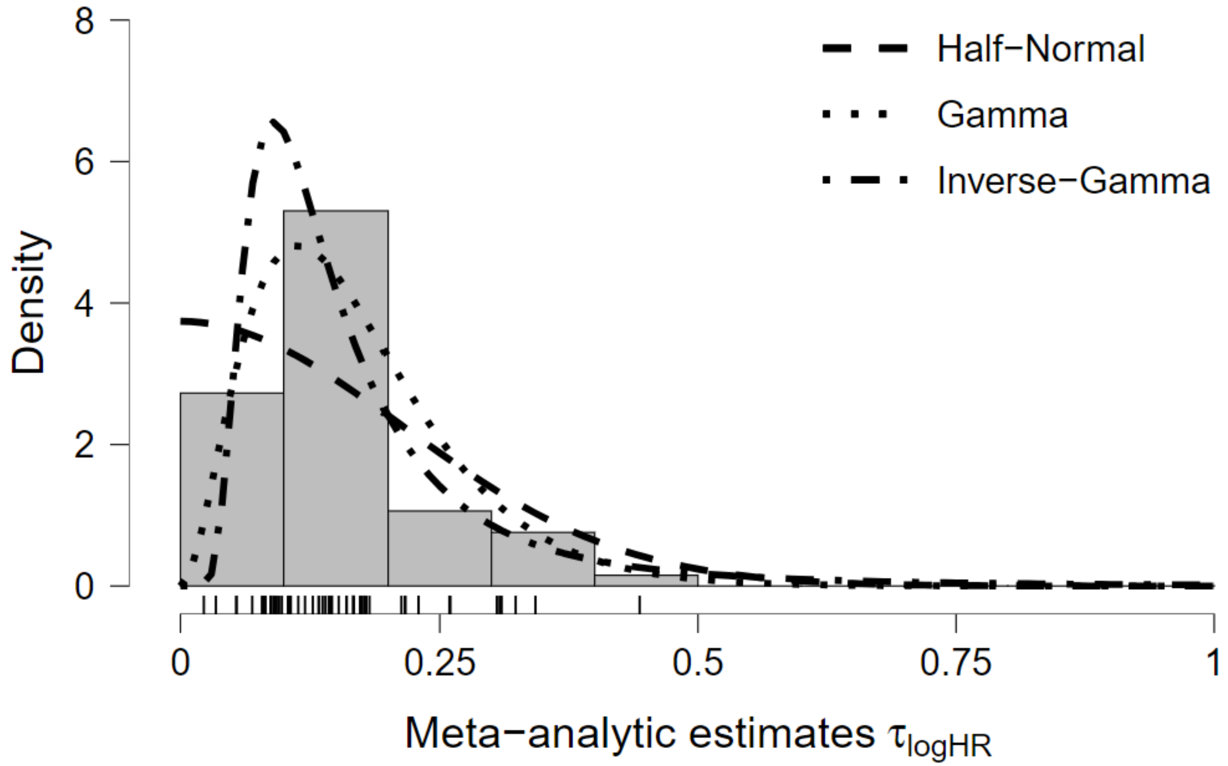




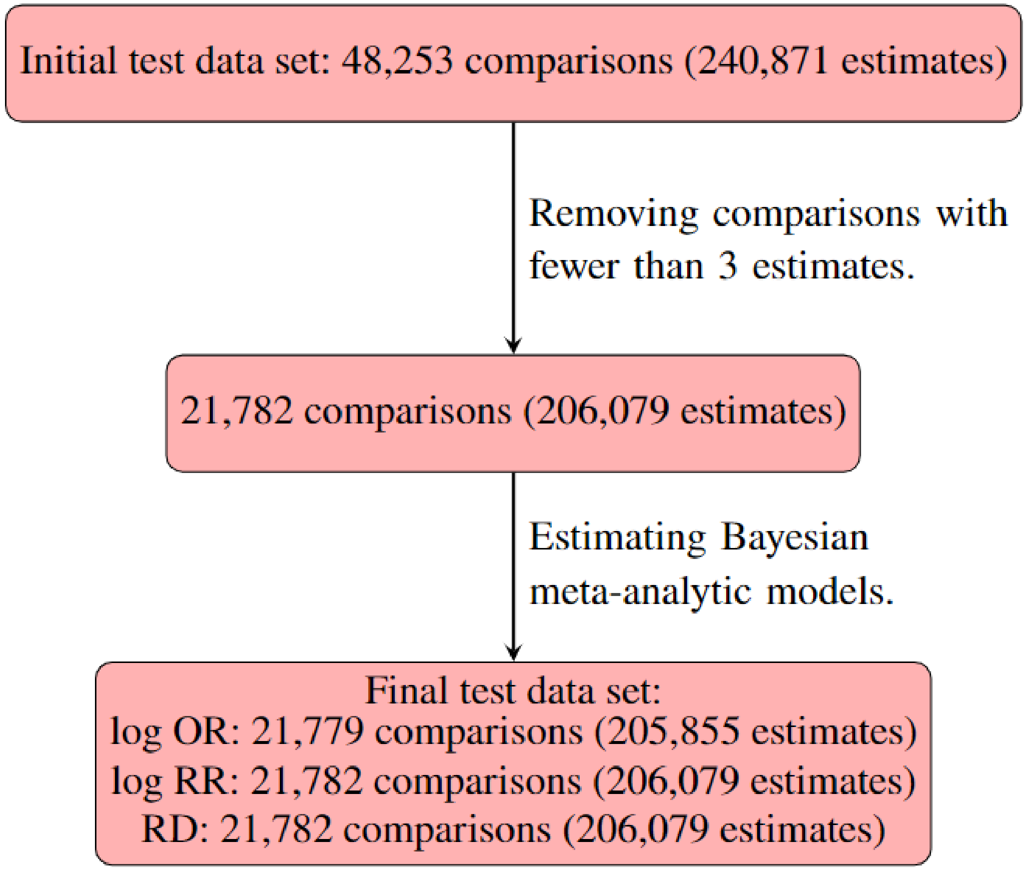
Prior Distributions for log HR

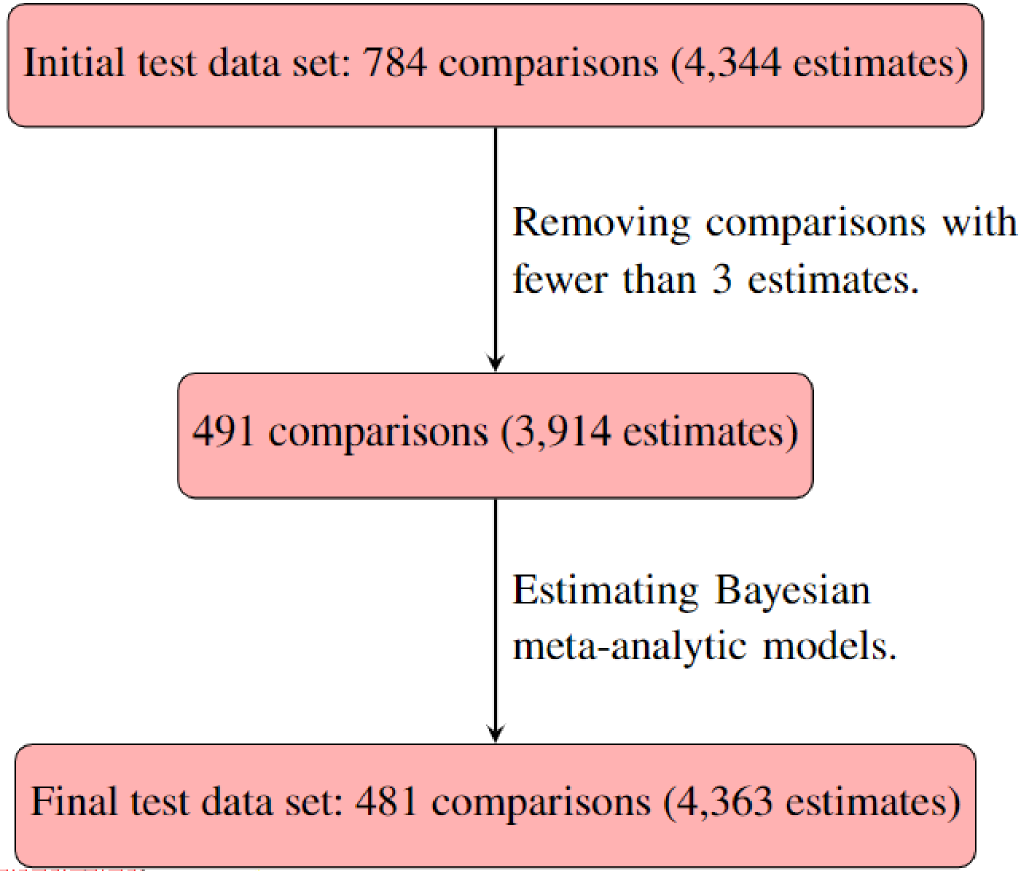
Time to event outcomes as log HR	
$\mu \sim \text{Normal}(0, 0.35)$	$\tau \sim \text{Normal}_{+}(0, 0.26)$
$\mu \sim \text{Student-t}(0, 0.21, 2.57)$	$\tau \sim \text{Inv-Gamma}(1.80, 0.21)$
	$\tau \sim \text{Gamma}(1.93, 0.11)$





Test Data Set





Binary outcomes as log OR

$\mu \sim \text{Student-t}(0, 0.78, 5)$	$\tau \sim \text{Inv-Gamma}(1.71, 0.73)$
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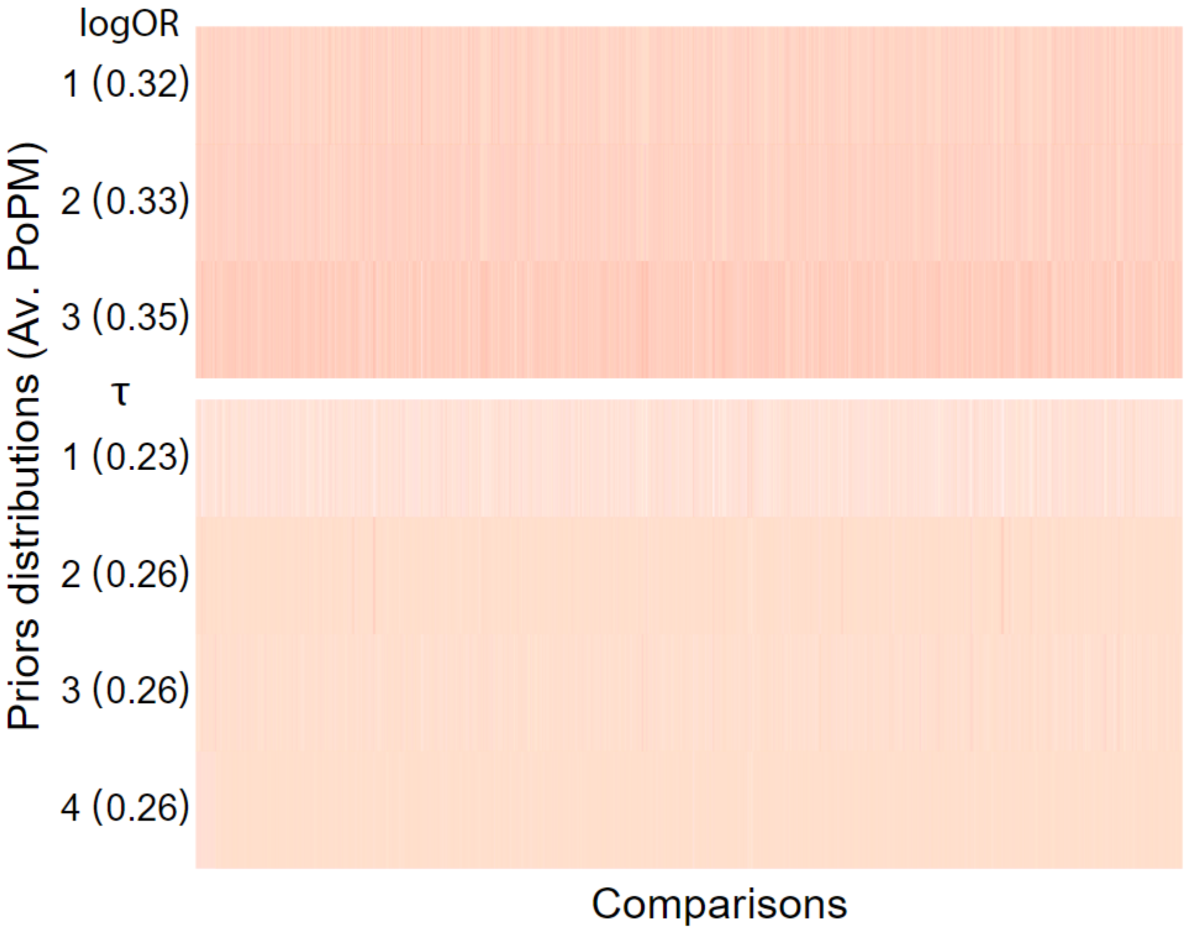

Time to event outcomes as log HR

$\mu \sim \text{Normal}(0, 0.35)$	$\tau \sim \text{Normal}_{+}(0, 0.26)$
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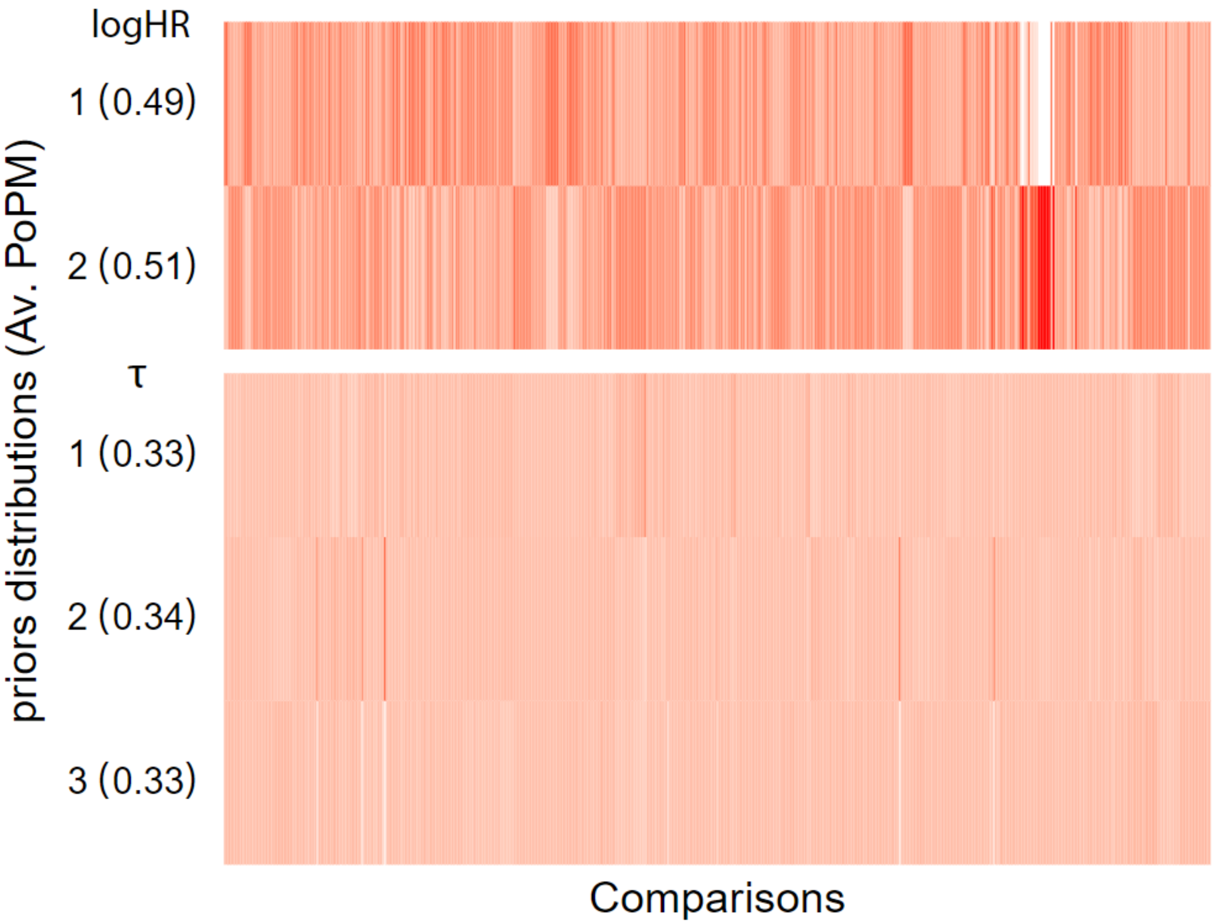
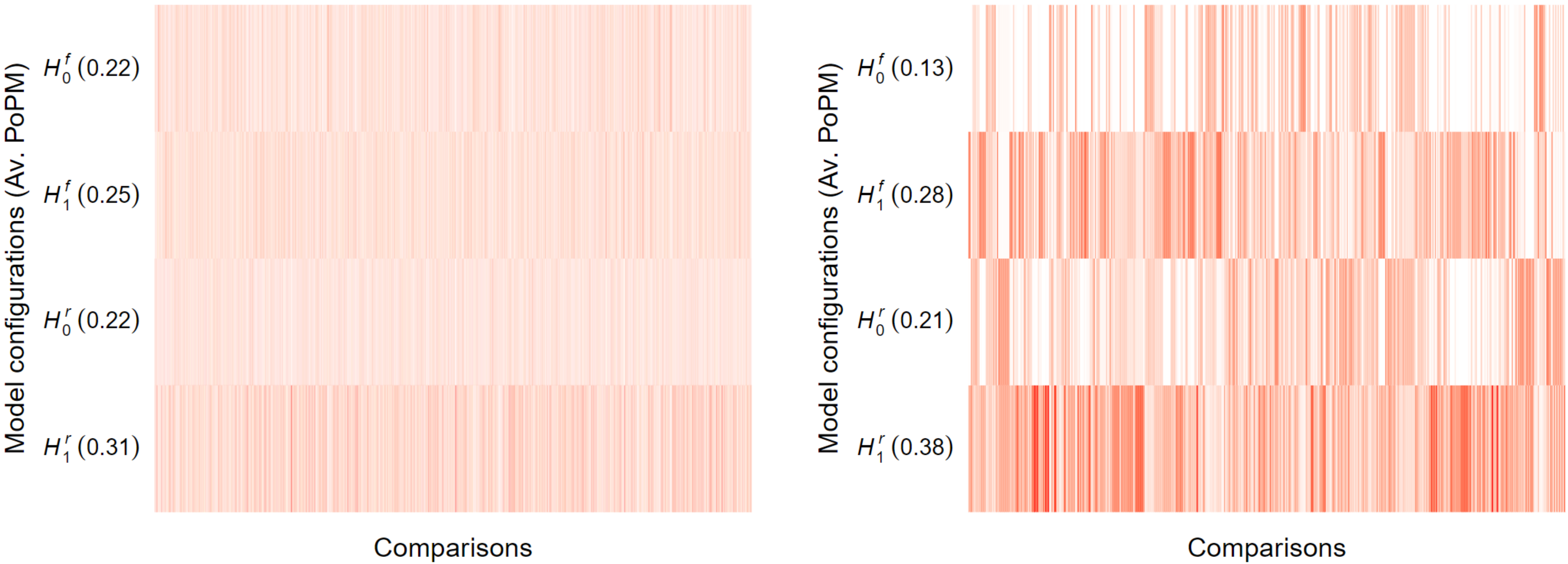



Model configurations (Av. PoPM)
H_0^f (0.22)
H_1^f (0.25)
H_0^r (0.22)
H_1^r (0.31)
Comparisons
Model configurations (Av. PoPM)
H_0^f (0.13)
H_1^f (0.28)
H_0^r (0.21)
H_1^r (0.38)
Comparisons

Topic	Comparisons μ	Comparisons τ	Prior μ	Prior τ
Acute Respiratory Infections	308 (5860)	197 (4061)	Student-t(0, 0.48, 3)	Inv-Gamma(1.67, 0.45)
Airways	450 (8702)	207 (3839)	Student-t(0, 0.37, 2)	Inv-Gamma(1.35, 0.27)
Anaesthesia	408 (9409)	261 (6781)	Student-t(0, 0.79, 6)	Inv-Gamma(2.12, 0.86)
Back and Neck	14 (295)	10 (238)	Student-t(0, 0.62, 4)	Inv-Gamma(1.84, 0.68)
Bone, Joint and Muscle Trauma	202 (3732)	103 (1937)	Student-t(0, 0.44, 2)	Inv-Gamma(1.01, 0.36)
Breast Cancer	137 (2646)	113 (2296)	Student-t(0, 0.39, 3)	Inv-Gamma(1.59, 0.48)
Childhood Cancer	1 (13)	—	Student-t(0, 0.47, 4)	—
Colorectal	230 (4120)	141 (2685)	Student-t(0, 0.65, 4)	Inv-Gamma(1.71, 0.60)
Common Mental Disorders	649 (13322)	422 (9731)	Student-t(0, 0.54, 4)	Inv-Gamma(1.63, 0.45)
Consumers and Communication	44 (918)	41 (875)	Student-t(0, 0.48, 4)	Inv-Gamma(2.37, 0.86)
Cystic Fibrosis and Genetic Disorders	81 (1843)	40 (964)	Student-t(0, 0.40, 3)	Inv-Gamma(1.82, 0.58)
Dementia and Cognitive Improvement	127 (2097)	78 (1278)	Student-t(0, 0.49, 4)	Inv-Gamma(1.28, 0.25)
Developmental, Psychosocial and Learning Problems	106 (1457)	79 (1083)	Student-t(0, 0.83, 5)	Inv-Gamma(1.83, 0.82)
Drugs and Alcohol	103 (2027)	73 (1545)	Student-t(0, 0.44, 4)	Inv-Gamma(1.59, 0.42)
Effective Practice and Organisation of Care	59 (1106)	44 (878)	Student-t(0, 0.51, 4)	Inv-Gamma(1.90, 0.68)
Emergency and Critical Care	233 (4803)	152 (3466)	Student-t(0, 0.35, 3)	Inv-Gamma(1.46, 0.34)
ENT	17 (243)	10 (136)	Student-t(0, 0.81, 4)	Inv-Gamma(1.73, 0.71)
Epilepsy	114 (2052)	39 (839)	Student-t(0, 0.88, 6)	Inv-Gamma(1.71, 0.43)
Eyes and Vision	57 (1007)	41 (815)	Student-t(0, 0.77, 5)	Inv-Gamma(2.09, 0.94)
Fertility Regulation	62 (1072)	46 (818)	Student-t(0, 0.46, 5)	Inv-Gamma(2.21, 0.71)
Gut	314 (6056)	215 (4595)	Student-t(0, 0.63, 5)	Inv-Gamma(1.94, 0.62)
Gynaecological, Neuro-oncology and Orphan Cancer	245 (5811)	159 (4123)	Student-t(0, 0.53, 4)	Inv-Gamma(1.80, 0.56)
Gynaecology and Fertility	364 (6896)	185 (3714)	Student-t(0, 0.40, 2)	Inv-Gamma(1.24, 0.28)
Haematology	155 (4546)	101 (3080)	Student-t(0, 0.57, 4)	Inv-Gamma(2.91, 0.66)
Heart	979 (20760)	579 (14085)	Student-t(0, 0.20, 2)	Inv-Gamma(1.64, 0.29)
Heart; Vascular	8 (178)	7 (166)	Student-t(0, 0.95, 4)	Inv-Gamma(1.64, 0.83)
Hepato-Biliary	1042 (36665)	706 (25668)	Student-t(0, 0.43, 3)	Inv-Gamma(1.58, 0.40)
HIV/AIDS	32 (475)	22 (293)	Student-t(0, 0.32, 4)	Inv-Gamma(1.76, 0.36)
Hypertension	66 (1127)	28 (453)	Student-t(0, 0.28, 5)	Inv-Gamma(1.25, 0.10)
Incontinence	78 (1479)	53 (1023)	Student-t(0, 0.75, 3)	Inv-Gamma(2.07, 1.09)
Infectious Diseases	361 (6619)	251 (4787)	Student-t(0, 0.66, 3)	Inv-Gamma(2.08, 0.86)
Injuries	214 (5662)	143 (4182)	Student-t(0, 0.60, 4)	Inv-Gamma(1.52, 0.49)
Kidney and Transplant	479 (8828)	274 (5226)	Student-t(0, 0.53, 4)	Inv-Gamma(1.68, 0.44)
Lung Cancer	76 (1416)	68 (1294)	Student-t(0, 0.61, 5)	Inv-Gamma(2.04, 0.68)
Metabolic and Endocrine Disorders	130 (3092)	78 (2190)	Student-t(0, 0.29, 2)	Inv-Gamma(0.92, 0.11)
Methodology	74 (2098)	69 (1997)	Student-t(0, 0.60, 5)	Inv-Gamma(2.04, 0.50)
Movement Disorders	59 (1058)	35 (708)	Student-t(0, 0.73, 5)	Inv-Gamma(2.14, 0.64)
Multiple Sclerosis and Rare Diseases of the CNS	29 (564)	23 (487)	Student-t(0, 0.76, 4)	Inv-Gamma(2.09, 0.71)
Musculoskeletal	139 (2403)	92 (1686)	Student-t(0, 0.59, 4)	Inv-Gamma(1.76, 0.59)
Neonatal	337 (6327)	153 (2738)	Student-t(0, 0.29, 3)	Inv-Gamma(1.80, 0.42)
Neuromuscular	43 (739)	20 (331)	Student-t(0, 0.70, 5)	Inv-Gamma(1.74, 0.49)
Oral Health	63 (990)	45 (724)	Student-t(0, 1.13, 4)	Inv-Gamma(1.85, 0.70)
Pain, Palliative and Supportive Care	315 (6062)	204 (4292)	Student-t(0, 1.00, 7)	Inv-Gamma(1.50, 0.40)
Pregnancy and Childbirth	1307 (24397)	832 (16588)	Student-t(0, 0.38, 2)	Inv-Gamma(1.73, 0.47)
Schizophrenia	609 (13515)	405 (9919)	Student-t(0, 0.58, 4)	Inv-Gamma(1.92, 0.69)
Sexually Transmitted Infections	25 (318)	19 (236)	Student-t(0, 0.61, 2)	Inv-Gamma(1.72, 0.47)
Skin	142 (2309)	76 (1294)	Student-t(0, 0.81, 2)	Inv-Gamma(1.64, 0.49)
Stroke	299 (5310)	131 (2357)	Student-t(0, 0.22, 2)	Inv-Gamma(1.36, 0.21)
Tobacco Addiction	213 (4990)	168 (4079)	Student-t(0, 0.49, 5)	Inv-Gamma(2.51, 0.63)
Urology	89 (1673)	60 (1271)	Student-t(0, 0.82, 5)	Inv-Gamma(1.72, 0.50)
Vascular	187 (2590)	116 (1711)	Student-t(0, 0.68, 5)	Inv-Gamma(1.70, 0.45)
Work	14 (208)	11 (178)	Student-t(0, 0.59, 4)	Inv-Gamma(1.79, 0.73)
Wounds	75 (1169)	53 (888)	Student-t(0, 0.60, 4)	Inv-Gamma(2.16, 0.86)
Pooled Estimate	11964 (253054)	7478 (170628)	Student-t(0, 0.58, 4)	Inv-Gamma(1.77, 0.55)

Example:
Adverse effects of honey in treating acute cough in children

Two studies with the comparison honey and no treatment on the presence of nervousness, insomnia, hyperactivity

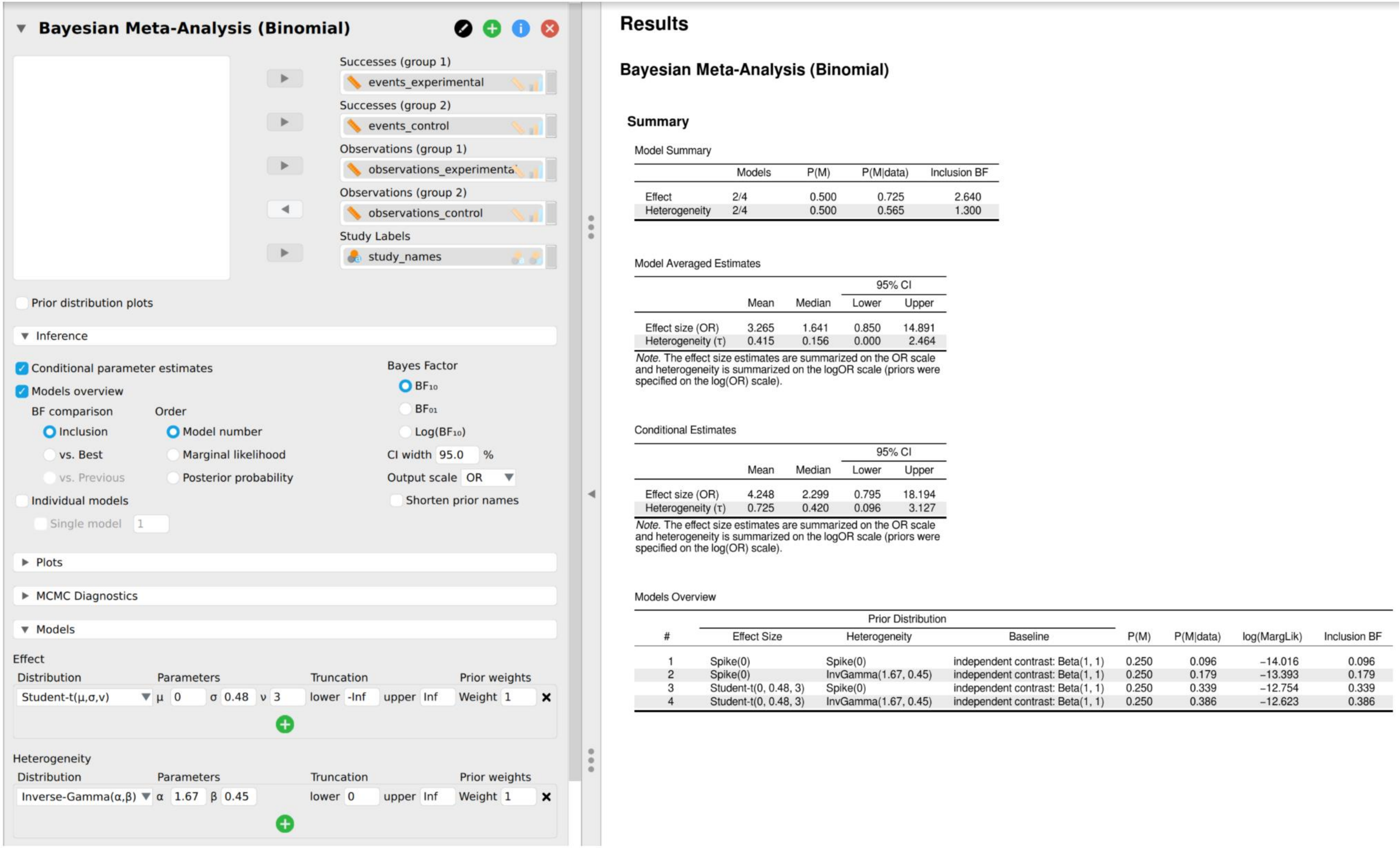
Honey condition: 5/35, 2/40 events

No treatment: 0/39, 0/40 events

Frequentist analysis: OR = 9.40, 95% CI [1.16, 76.20], z = 2.10, p = 0.04

Oduwole, O., Udoh, E. E., Oyo-Ita, A., & Meremikwu, M. M. (2018). Honey for acute cough in children. *Cochrane Database of Systematic Reviews*, (4).

```
> library("RoBMA")

> fit <- BiBMA(
  x1 = events_experimental,
  x2 = events_control,
  n1 = observations_experimental,
  n2 = observations_control,
  priors_effect        = prior(distribution="t", parameters=list(location=0, scale=0.48, df=3)),
  priors_heterogeneity = prior(distribution="invgamma", parameters=list(shape=1.67, scale=0.45)),
  seed = 1)

> summary(fit, conditional = TRUE, output_scale = "OR")

Bayesian model-averaged meta-analysis (binomial-normal model)
Components summary:
              Models Prior prob. Post. prob. Inclusion BF
Effect           2/4       0.500       0.725        2.630
Heterogeneity    2/4       0.500       0.564        1.296

Model-averaged estimates:
     Mean Median 0.025  0.975
mu  3.389  1.642 0.842 15.143
tau 0.420  0.158 0.000  2.594

Conditional estimates:
     Mean Median 0.025  0.975
mu  4.242  2.261 0.781 17.613
tau 0.747  0.426 0.097  3.233
The effect size estimates are summarized on the OR scale and heterogeneity is summarized on the logOR scale
(priors were specified on the log(OR) scale).
```



Bayesian Meta-Analysis (Binomial)

Summary

Model Summary

	Models	P(M)	P(M|data)	Inclusion BF
Effect	2/4	0.500	0.725	2.640
Heterogeneity	2/4	0.500	0.565	1.300

Model Averaged Estimates

			95% CI	
	Mean	Median	Lower	Upper
Effect size (OR)	3.265	1.641	0.850	14.891
Heterogeneity (τ)	0.415	0.156	0.000	2.464

Note. The effect size estimates are summarized on the OR scale and heterogeneity is summarized on the logOR scale (priors were specified on the log(OR) scale).

Conditional Estimates

			95% CI	
	Mean	Median	Lower	Upper
Effect size (OR)	4.248	2.299	0.795	18.194
Heterogeneity (τ)	0.725	0.420	0.096	3.127

Note. The effect size estimates are summarized on the OR scale and heterogeneity is summarized on the logOR scale (priors were specified on the log(OR) scale).

Models Overview

	Prior Distribution						
#	Effect Size	Heterogeneity	Baseline	P(M)	P(M|data)	log(MargLik)	Inclusion BF
1	Spike(0)	Spike(0)	independent contrast: Beta(1, 1)	0.250	0.096	−14.016	0.096
2	Spike(0)	InvGamma(1.67, 0.45)	independent contrast: Beta(1, 1)	0.250	0.179	−13.393	0.179
3	Student-t(0, 0.48, 3)	Spike(0)	independent contrast: Beta(1, 1)	0.250	0.339	−12.754	0.339
4	Student-t(0, 0.48, 3)	InvGamma(1.67, 0.45)	independent contrast: Beta(1, 1)	0.250	0.386	−12.623	0.386

Conclusions

- Differentiating between absence of evidence vs. evidence of absence
- Incorporating uncertainty about the specified model
- Incorporating historical knowledge
- Better convergence properties
- Sequential updating of evidence

Thank You for Your Attention

- Preprint: https://arxiv.org/abs/2306.11468
- R-package: https://cran.r-project.org/package=RoBMA
- JASP: https://jasp-stats.org/