Meta-Analysis to Meta-Cognition

Following the Bayesian Highway

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Learning Objectives

0:00 / 5:01

Baba Brinkman - Good Bayesian

1. Understanding Bayesian Meta-analysis -> Why Bayesian inference matters in evidence synthesis
2. Developing Meta-cognition Skills -> Make assumptions explicit; account for uncertainty; set minimally clinically important difference (MCID); report $P(\mu \leq MCID))$ -> better decisions
3. Application to clinical examples -> Compute, visualize, -> decisions (benefit vs. harm/cost)
    - Colchicine post-ACS
    - Extended thrombolysis in acute ischemic stroke
    - Dexmedetomidine and post-operative delirium

What is Meta-Analysis** (MA)?

- Statistical method combines multiple studies to estimate a common effect, θ and between-study variation, τ
- Very common (≈ 30,000 publications with MA in title so far in 2025)
- Common MA methods (frequentist) have limitations / assumptions
  - θ is a fixed (but unknown) constant, (only data are random)
  - Thus 95% CI is a property of the data procedure, not of θ
  - IOW, if study repeated many times, 95% of intervals would cover θ
  - Ignores prior ancillary θ knowledge
  - Favors dichotomous arbitrary decision thresholds ($p < 0.05$)
  - No probability statements about θ or answer clinical questions like:
    - "How likely is the effect big enough to matter in my setting?"

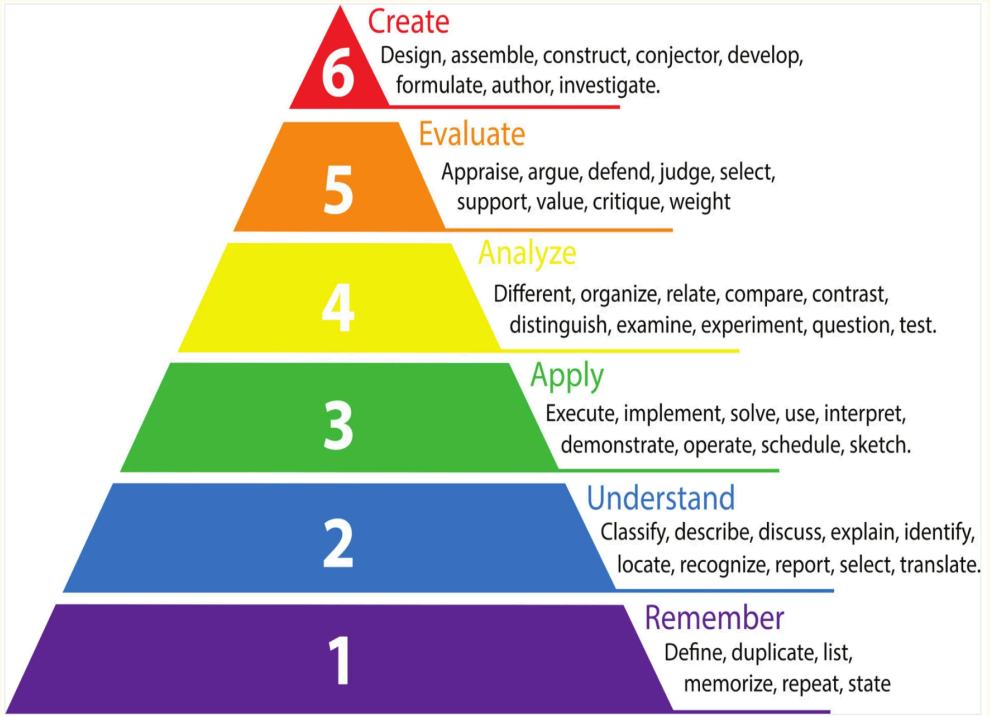
meta — prefix of Greek origin meaning "after, higher, beyond"

What is Meta-Cognition?

- **Meta-cognition** = thinking about thinking
- Traditional inference asks: “Is there an effect?”
- Meta-cognition extends with purposeful reflection and situational awareness:
  - “Is the effect large enough to matter?”
  - “What should I do given this evidence?”
- For example: RR = 0.82 with 95% CrI [0.66, 1.03], p = 0.11†
  - Recognize p > 0.05 doesn’t imply clinical irrelevance
  - Should you act, wait, or gather more evidence?
  - Probability benefit > my minimally clinically important difference (MCID) threshold?

† POPular (AGE), *Lancet* 2020

Taxonomy of Learning



Overview Of Bloom's Taxonomy

- Meta-cognition - Reflects Bloom's top tiers
- Evidence → Insight (evaluate) → Action (create)
- Enables clinicians to:
  - Question assumptions
  - Integrate uncertainty
  - Move beyond binary decisions (significant vs not)
  - Tailor decisions (shared, informed) to context

Meta-Cognition and Bayesian Meta-Analysis

Meta-cognition: the **destination** — clinical wisdom beyond the numbers, deeper understanding, communication and wiser decisions

Bayesian meta-analysis: the **statistical engine** (the GPS) - **navigating uncertainty with purpose** - to get to our destination

Why Bayesian?

- Principled accounting of uncertainty → uncertainty that propagates throughout the model
- Combines data & prior information → weak/elastic priors stabilize small / zero-event datasets
- Models what matters → complex data generating processes, hierarchies, biases, etc
- Informed decisions making → full posterior distributions probabilities (e.g., $(P(\mu \leq -MCID))$, no dichotomized p values
- Shrinkage & robustness → partial pooling improved inferences about individual studies

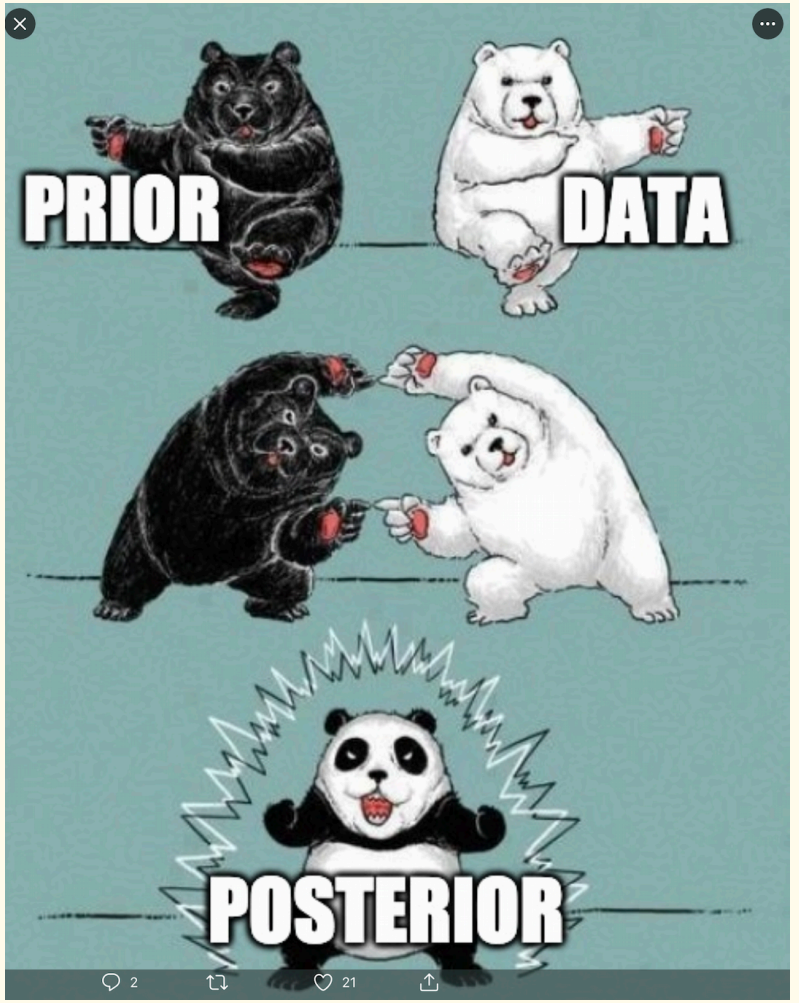
"Bayesian inference - what you do when you believe you should condition on what you know." — Andrew Gelman

Small caveats
- Results can be prior-sensitive when data are thin — need robustness checks
- Computation/communication can be heavier (but analytic/conjugate or Laplace paths often make it light)

Bayesian Key Concept

$$\text{Posterior} \propto \text{Likelihood} \times \text{Prior}$$

- Prior: What you believe **before** the new evidence
- Likelihood: What the new data say
- Posterior: What you believe **after** combining both



Prior Knowledge: A Strength or Limitation (Bias)?

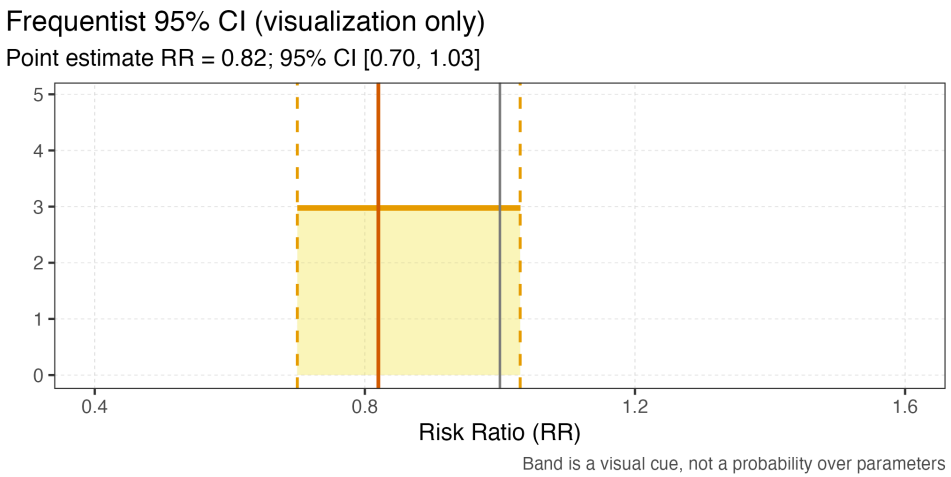
- Strength: Informs probabilistic inference, enables cumulative learning
- Criticism: “Subjective”
- Response:
  - All models involve assumptions
  - Assumptions can be tested
  - Bayesianism just makes assumptions (priors) explicit

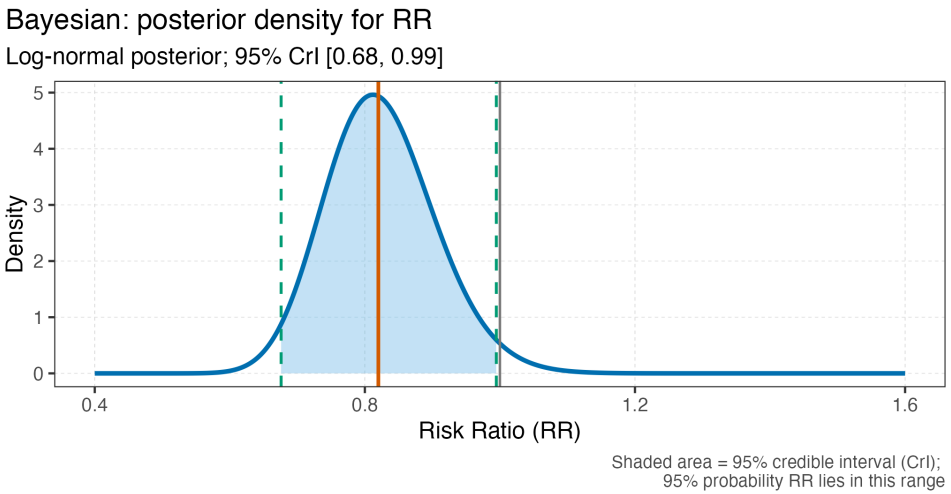
Frequentist vs Bayesian Meta-analysis

Feature	Frequentist	Bayesian
Point estimate	Yes	Yes
Confidence/Credible Interval	CI (coverage probability)	CrI (posterior probability)
Interpretations	Long-run frequency: 95% of intervals cover true effect	95% chance the true effect lies within the interval
Parameter interpretation	Fixed (unknown constant)	Random variable with probability
Probability Statements	Not valid for individual studies or patients	Directly answer “how likely” questions
Shrinkage	No	Yes (esp. in hierarchical models)
Predictive intervals	Limited (available in mixed models)	Yes (posterior predictive distribution)
Prior inclusion	No	Yes
Tailored Inference	No	Yes (e.g., P(RR < 0.9), threshold-specific)

These differences matter

Consider previous RR 0.82 95% CI 0.66, 1.03, p = 0.11, what does this mean?





Frequentist CI -
- Long-run: 95% of CIs cover the fixed true RR if studies repeated
- This single CI either covers or not
- No probabilities, all values inside equally compatible with data
- 95% CI = set of values **not rejected** by α level-0.05 test with these data.

Bayesian CrI -
- 95% probability RR in the CrI (given prior + data)
- Values are ranked(centre > edges)
- Compute $(P(\mathrm{RR} \leq \mathrm{CID}))$ for decisions

MA Predictive Thinking: The Next Study

Pooled average = typical average effect across included studies

Predictive interval = likely next-study range (includes between-study heterogeneity, τ^2), i.e. effect is to be expected in future study / patients

Prediction intervals should be routinely reported (1,2)

Reference:

1. Riley RD, Higgins JPT, Deeks JJ. Interpretation of random effects meta-analyses. BMJ 2011;342:d549.

2. IntHout, J., J. P. Ioannidis, M. M. Rovers, and J. J. Goeman. "Plea for Routinely Presenting Prediction Intervals in Meta-Analysis." BMJ Open 6, no. 7 (Jul 12 2016)

MA Predictive Thinking: The Next Study

Frequentist

- Parameters are **fixed**, data are **random** -> probability statements about the true effect are **not defined**
- Prediction interval = future observation given fixed parameters
- Interpretation:
  > "There is a 95% chance that the next study's outcome falls within this interval, *if* the parameters are correct"

Bayesian

- Parameters are **random variables** with distributions, data is **fixed** → probability statements *about the effect* are **valid**
- Posterior predictive distribution integrates over parameter uncertainty
- Interpretation:
  > "There is a 95% probability that the next study's outcome lies in this range, *given our data and prior*."

Minimally Clinically Important Difference (MCID)

MCID probabilities only available with Bayesian approach

- Define a MCID based on clinical context:
  - e.g., ARR ≥ 1.5% over 3 years (RR ≤ 0.85 if baseline risk = 10%)
- Report:
  - P(RR < 1.0) (any benefit)
  - P(RR ≤ MCID) (clinically meaningful benefit)
  - Predictive interval for a new, comparable study
- Decision:
  - treat when P(RR ≤ CID) is high and the predictive interval lies mostly on the favorable side.

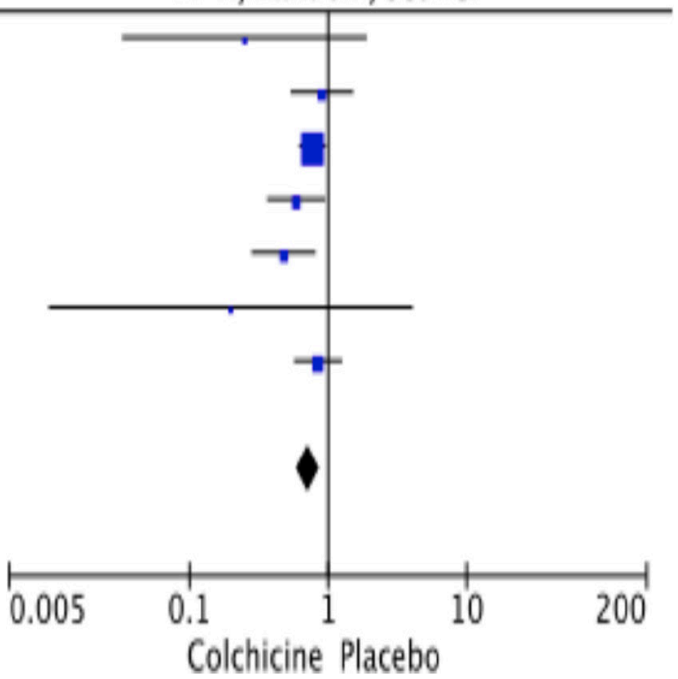
Colchicine in ACS

Colchicine's role in post-ACS care - a 2022 frequentist meta-analysis

Study or Subgroup	Colchicine Events	Colchicine Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
CISR	1	30	8	60	0.7%	0.25 [0.03, 1.91]
COLCHICINE-PCI	24	206	25	194	10.6%	0.90 [0.53, 1.53]
COLCOT	131	2366	170	2379	48.3%	0.77 [0.62, 0.97]
COPS	24	396	41	399	12.3%	0.59 [0.36, 0.96]
Deftereos 2013	16	100	32	96	10.3%	0.48 [0.28, 0.82]
Lodoco-MI	0	119	2	118	0.3%	0.20 [0.01, 4.09]
O'Keefe 1992	41	130	25	67	17.5%	0.85 [0.57, 1.26]
Total (95% CI)		**3347**		**3313**	**100.0%**	**0.73 [0.61, 0.87]**
Total events	237		303			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 6.37$, df = 6 (P = 0.38); $I^2 = 6\%$

Test for overall effect: Z = 3.58 (P = 0.0003)



Conclusion: Colchicine "significantly" reduced the risk of MACE in CAD patients

Is the colchicine / ACS story over, or is further research justified or even ethical?

Not so fast...

- No prediction interval (PI) for next study provided
- Frequentist PI (0.60 - 0.90) assumes study parameters & statistical model are known without uncertainty -> overconfident conclusions
- Bayesian PI for next study accounts for parameter variability -> CI 0.35 - 1.29
- Providing more realistic heterogeneity estimate and justification for future studies

CLEAR Trial: Colchicine in ACS

NEJM 2025 publication, investigators obviously didn't believe the colchicine story was over

So are the investigators Bayesian?

- 7062 patients randomized at 104 centers in 14 countries
- Primary outcome: CV death, MI, stroke, or urgent revascularization
- Results: RR = 0.99 (95% CI 0.85–1.16, p=0.93)

Conclusion: "Treatment with colchicine, when started soon after MI and continued for a median of 3 years, did not reduce theincidence of the composite primary outcome."

Colchine Meta-Analyses in 2025

CLEAR acknowledged previous COLCOT RCT (n = 4725, HR 0.77, 95% CI 0.61 - 0.96)
No effort to quantitatively incorporate or explain this, or any other, study results
Simply stated CLEAR was a larger trial, with an improved precision

So definitely not Bayesians!

7 meta-analyses have been published in the 3-6 months following CLEAR!

All concluded colchicine is beneficial in post-ACS patients

PubMed: Search: colchicine AND coronary disease Filters: Meta-Analysis, from 2025/1/1 - 2025/7/24

References:

1. Younas et al. Curr Probl Cardiol 2025;50(1):102878. (In eng). DOI: 10.1016/j.cpcardiol.2024.102878.

2. Wang et al. Medicine (Baltimore) 2025;104(22):e42650. (In eng). DOI: 10.1097/md.0000000000042650.

3. Shaikh et al. Int J Cardiol 2025;425:133045. (In eng). DOI: 10.1016/j.ijcard.2025.133045.

4. Samuel et al. Eur Heart J 2025;46(26):2552-2563. (In eng). DOI: 10.1093/eurheartj/ehaf174.

5. Jaiswal et al.Am J Cardiovasc Drugs 2025;25(1):83-93. (In eng). DOI: 10.1007/s40256-024-00689-7.

6. Ballacci et al.J Cardiovasc Med (Hagerstown) 2025;26(7):359-368. (In eng). DOI: 10.2459/jcm.0000000000001744.

7. d'Entremont et al. Eur Heart J 2025;46(26):2564-2575. (In eng). DOI: 10.1093/eurheartj/ehaf210.

Colchicine Meta-Analyses in 2025

EHJ - IF 36.4

Colchicine for secondary prevention of vascular events: a meta-analysis of trials

Marc-André d'Entremont [1,2,3,†], Michiel H.F. Poorthuis[4], Aernoud T.L. Fiolet[5,6], Pierre Amarenco[1,7], Kevin Emery Boczar[8], Ian Buysschaert[9], Noel C. Chan [10], Jan H. Cornel[6,11,12], Jalina Jannink[13], Shirley Jansen[14], Sasko Kedev[15], Anthony C. Keech[16,17], Jamie Layland[18], Nathan Mewton[19], Gilles Montalescot[20], Domingo A. Pascual-Figal[21,22], Alfredo E. Rodriguez[23], Binita Shah[24,25], Martin Teraa [26], Aimee van Zelm[26], Yongjun Wang[27], Arend Mosterd [6,13], Peter Kelly[28,29], John Eikelboom[1,30], and Sanjit S. Jolly[1,2,*]; on behalf of the Colchicine Cardiovascular Trialists Collaboration

- "In 2^o prevention, colchicine reduced the composite outcome by 12%"
- Includes CLEAR authors and published only 3 months after CLEAR trial
- Apparently frequentist statistics allows investigators to declare both that the treatment does not, and simultaneously does work, all with same available evidence!!!

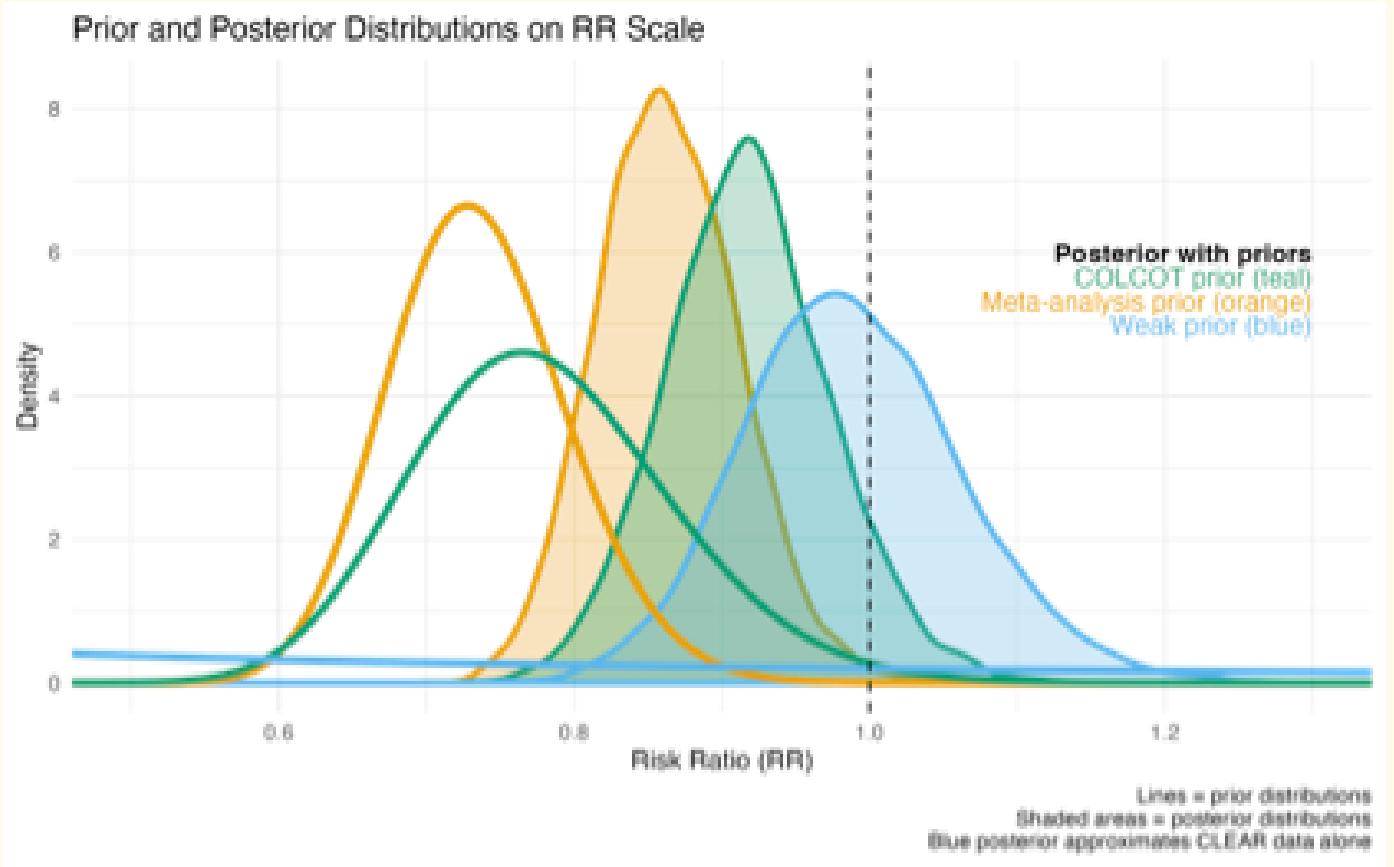
Anatomy of a Bayesian Meta-Analysis

1. Standard difficulties - searching relevant studies & critical quality assessment (GIGO)
2. Additional difficulty - define the priors
3. Specify model (random or fixed effects, bias corrections)
4. Combine likelihood from all studies to compute posterior (via MCMC)
5. Interpret full distribution, not just point estimate

```r
# brms example for Bayesian meta-analysis
library(brms)
brm(r | trials(n) ~ 0 + treatment + (1 | Study),
    family = binomial(),
    data = nma_data,
    prior = prior(normal(0, 2), class = b),
    chains = 4, cores = 4)
```

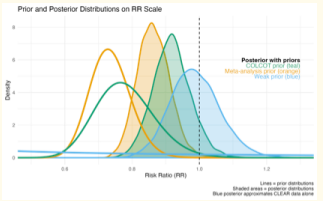
Colchicine Prior Beliefs: Three Perspectives

- Use a community of prior beliefs to assess conclusions' robustness
- Vague prior: N(0, 2) → allows CLEAR data to dominate
- Focused prior: Based on major pre-CLEAR trial – COLCOT as acknowledged by CLEAR
- Comprehensive prior: Based on 2022 meta-analysis (pre-CLEAR)



- Posterior mean RR:
  - Vague: 0.99 (95% CrI 0.85–1.14)
    P(RR<1 = 58%)
  - Focused (COLCOT): 0.92 (0.81–1.03)
    P(RR<1 = 92%)
  - Comprehensive (2022 MA): 0.86 (0.78–0.96)
    P(RR<1 = 100%)

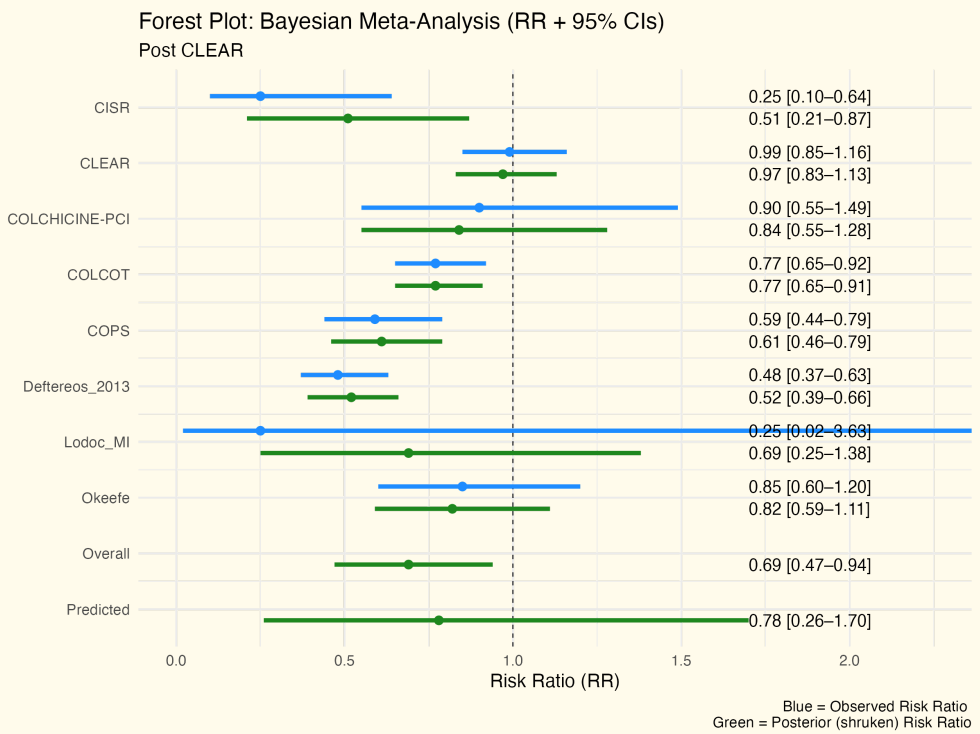
Probabilities for Clinical Thresholds



Prior	P(RR < 0.8)	P(RR < 0.85)	P(RR < 0.9)	P(RR < 1.0)	P(RR < 1.15)
Weak (N(0,2))	0%	3%	11%	58%	98%
COLCOT-based	1%	11%	38%	92%	100%
Meta-analysis	9%	40%	78%	100%	100%

1. CLEAR & weak prior-> modest 58% probability of some benefit (RR < 1.0)
2. COLCOT & meta-analysis priors -> higher probability of some benefit (92-100%) but only modest probability (11-40%) of clinical significance (RR < 0.85).
3. Predictive spread next study is CI 0.26 - 1.70 —> substantial residual uncertainty
4. More informed than frequentist 12% reduction with no uncertainty measure

Bayesian forest plot



- Partial pooling -> shrinkage extreme trials
- Bayesian models pull estimates toward the mean
- Particularly helpful in small trials or sparse data
- Hierarchical model accounts for heterogeneity
- Colchicine example - Bayesian next study: RR 0.78, 0.26–1.70 (wider, more realistic than frequentist PI)

What this means for practice today

- CLEAR (RR ~0.99, p = 0.93) ≠ proof of no effect
- Absence of evidence ≠ evidence of absence
- Frequentist meta-analysis: 12% reduction but no measure of uncertainty
- Bayesian analysis: ~60–100% probability RR < 1 but only modest (~11-40%) probability of ≥15% benefit
- The evidence does not completely reject the colchicine hypothesis — but does rule out high probability of any very strong benefit
- Reasonable decisions for colchicine post-ACS
  1. Wait for more evidence, especially if your MCID is ≥15% RRR
  2. Targeted use in higher-risk groups + honest discussion of uncertainty if your MCID is < 15% RRR

Extended thrombolysis in acute ischemic stroke

- Guidelines recommend thrombolysis within a 4.5-hour time window from sx onset
- Six RCTs with guided advanced neuroimaging of extended thrombolysis (> 4.5h since sx onset)
- Seven published MAs!!!! all concluded benefit

Original RCTs:

1. Thomalla G, Simonsen CZ, Boutitie F, et al. MRI-guided thrombolysis for stroke with unknown time of onset. New England Journal of Medicine 2018;379(7):611-622.
2. Ma H, Campbell BC, Parsons MW, et al. Thrombolysis guided by perfusion imaging up to 9 hours after onset of stroke. New England Journal of Medicine 2019;380(19):1795-1803.
3. Koga M, Yamamoto H, Inoue M, et al. Thrombolysis with alteplase at 0.6 mg/kg for stroke with unknown time of onset: a randomized controlled trial. Stroke 2020;51(5):1530-1538.
4. Ringleb P, Bendszus M, Bluhmki E, et al. Extending the time window for intravenous thrombolysis in acute ischemic stroke using magnetic resonance imaging-based patient

Meta-analyses:

1. Roaldsen MB, Lindekleiv H, Mathiesen EB, Berge E. Recanalisation therapies for wake-up stroke. Cochrane Database of Systematic Reviews 2018(8).
2. Campbell BC, Ma H, Ringleb PA, et al. Extending thrombolysis to 4· 5–9 h and wake-up stroke using perfusion imaging: a systematic review and meta-analysis of individual patient data. The Lancet 2019;394(10193):139-147.
3. Thomalla G, Boutitie F, Ma H, et al. Intravenous alteplase for stroke with unknown time of onset guided by advanced imaging: systematic review and meta-analysis of individual patient data. The Lancet 2020;396(10262):1574-1584.

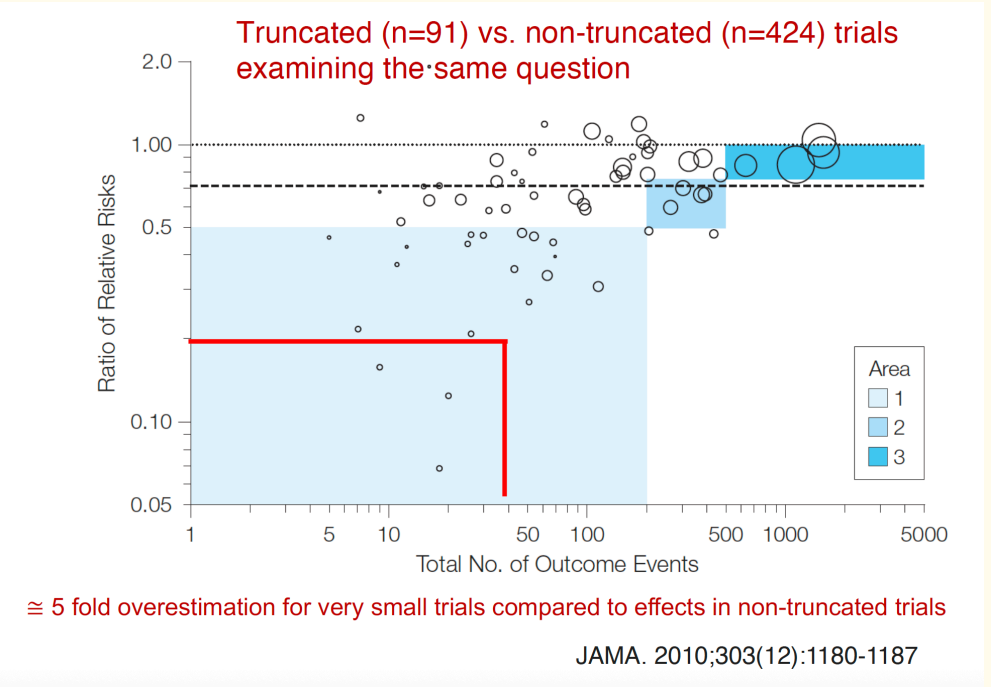
The RCTs

Remember: GIGO - garbage in, garbage out

Cochrane ROB 2.0 - some concerns in all trials

Trial	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Bias	Comments
WAKE-UP (2018)[6]	+	+	+	+	+	−	• Premature termination. • Seven investigators with FCOI
ECASS-4 (2019)[9]	+	+	+	+	+	−	• Premature termination. • Trial funded by drug manufacturer
EXTEND (2019)[7]	+	+	+	+	+	−	• Premature termination. • Seven investigators with FCOI
THAWS (2020)[8]	+	−	+	+	+	−	• Open label treatment. • Premature termination. Seven investigators with FCOI
TRACE-III	−	−	+	+	+	−	• 9 baseline characteristics favored the teneceplase • Observed allocation imbalance • Open label treatment. • Trial partially sponsored by the drug manufacturer.

Bias with early termination for benefit - overestimates effect size



≅ 5 fold overestimation for very small trials compared to effects in non-truncated trials

JAMA. 2010;303(12):1180-1187

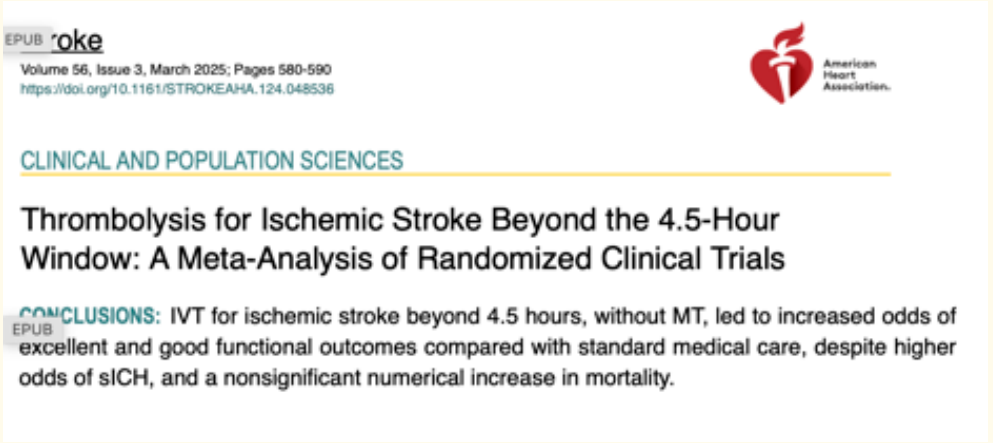
The outcome measure

Modified Rankin score - dichotomized at 0-1 vs 2-6 - losses information

Score	
0	No symptoms at all.
1	No significant disability despite symptoms; able to carry out all usual duties and activities.
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance.
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance.
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention.
6	Dead

Typical meta-analysis

Supportive of benefit



EPUB roke

Volume 56, Issue 3, March 2025; Pages 580-590
https://doi.org/10.1161/STROKEAHA.124.048536

American Heart Association.

CLINICAL AND POPULATION SCIENCES

Thrombolysis for Ischemic Stroke Beyond the 4.5-Hour Window: A Meta-Analysis of Randomized Clinical Trials

EPUB CONCLUSIONS: IVT for ischemic stroke beyond 4.5 hours, without MT, led to increased odds of excellent and good functional outcomes compared with standard medical care, despite higher odds of sICH, and a nonsignificant numerical increase in mortality.

Limitations

- Used dichotomized mRS - loses information
- Ordinal regression with utility weighting preferred outcome
- Inability to formulate meaningful probability statements
- e.g. “Nonsignificant increase in mortality” is not the same as “No increase in mortality”

utility-weighted mRS ordinal outcome

A UW-mRS similar to the standard ordinal mRS
Ensures quantitative outcome a valid reflection of patient-centered benefits / values

Utility weights <- c(1.00, 0.91, 0.76, 0.65, 0.33, 0.00, 0.00)

MCID threshold for the uw-mRS scale is ≥.09

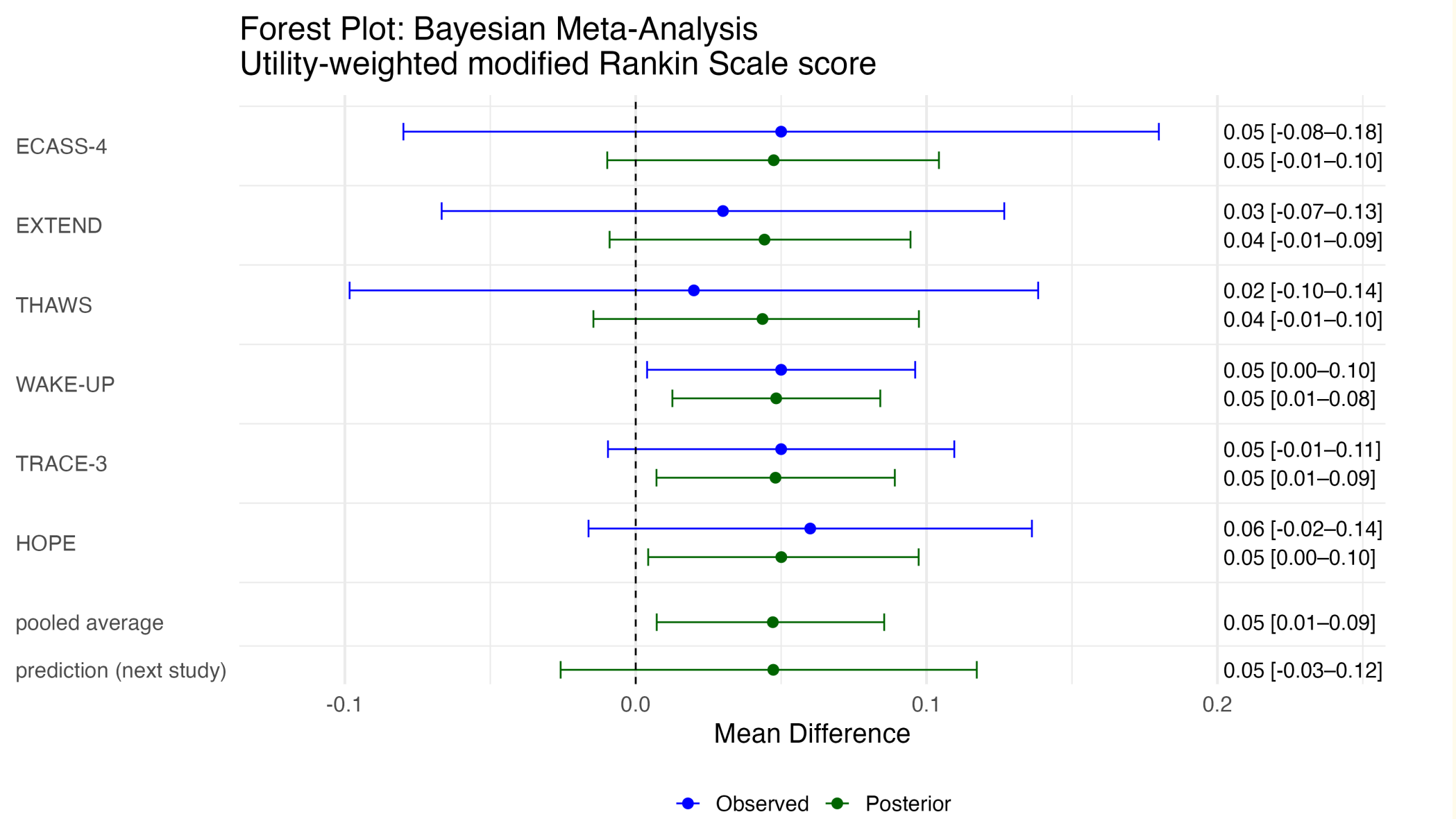
Reference:

1. Chaisinanunkul N, Adeoye O, Lewis RJ, et al. Adopting a patient-centered approach to primary outcome analysis of acute stroke trials using a utility-weighted modified Rankin scale. Stroke 2015;46(8):2238-2243 2.Zhou J, Wei Q, Hu H, et al. A systematic review and meta-analysis of health utility values among patients with ischemic stroke. Frontiers in Neurology 2023;14:1219679.

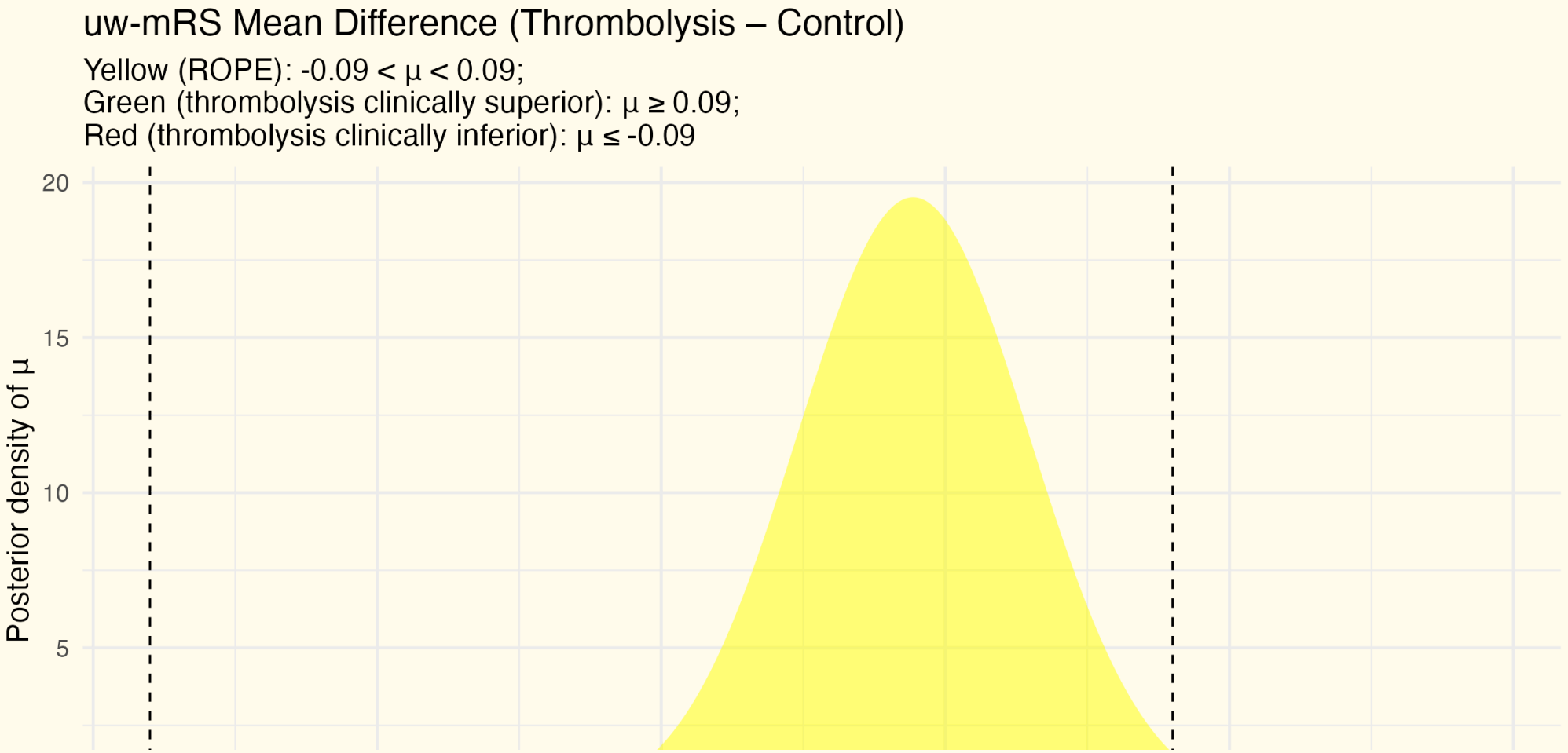
3. Chen P, Lin K-C, Liing R-J, Wu C-Y, Chen C-L, Chang K-C. Validity, responsiveness, and minimal clinically important difference of EQ-5D-5L in stroke patients undergoing rehabilitation. Quality of life research 2016;25:1585-1596.

4. Kim S-K, Kim S-H, Jo M-W, Lee S-i. Estimation of minimally important differences in the EQ-5D and SF-6D indices and their utility in stroke. Health and Quality of Life Outcomes 2015;13:1-6

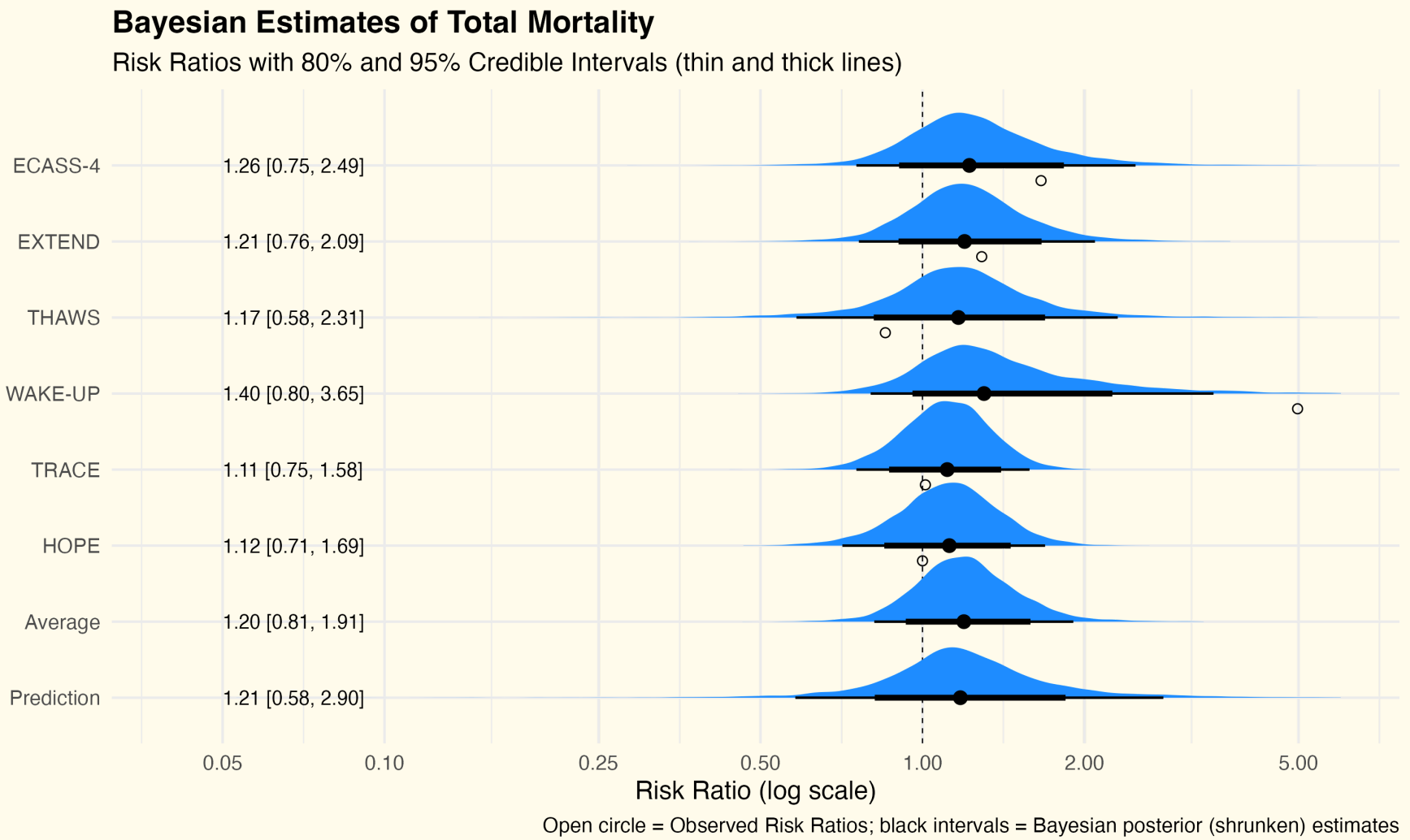
Bayesian MA of UW-mRS



Bayesian MA of UW-mRS



Bayesian mortality (relative risk)



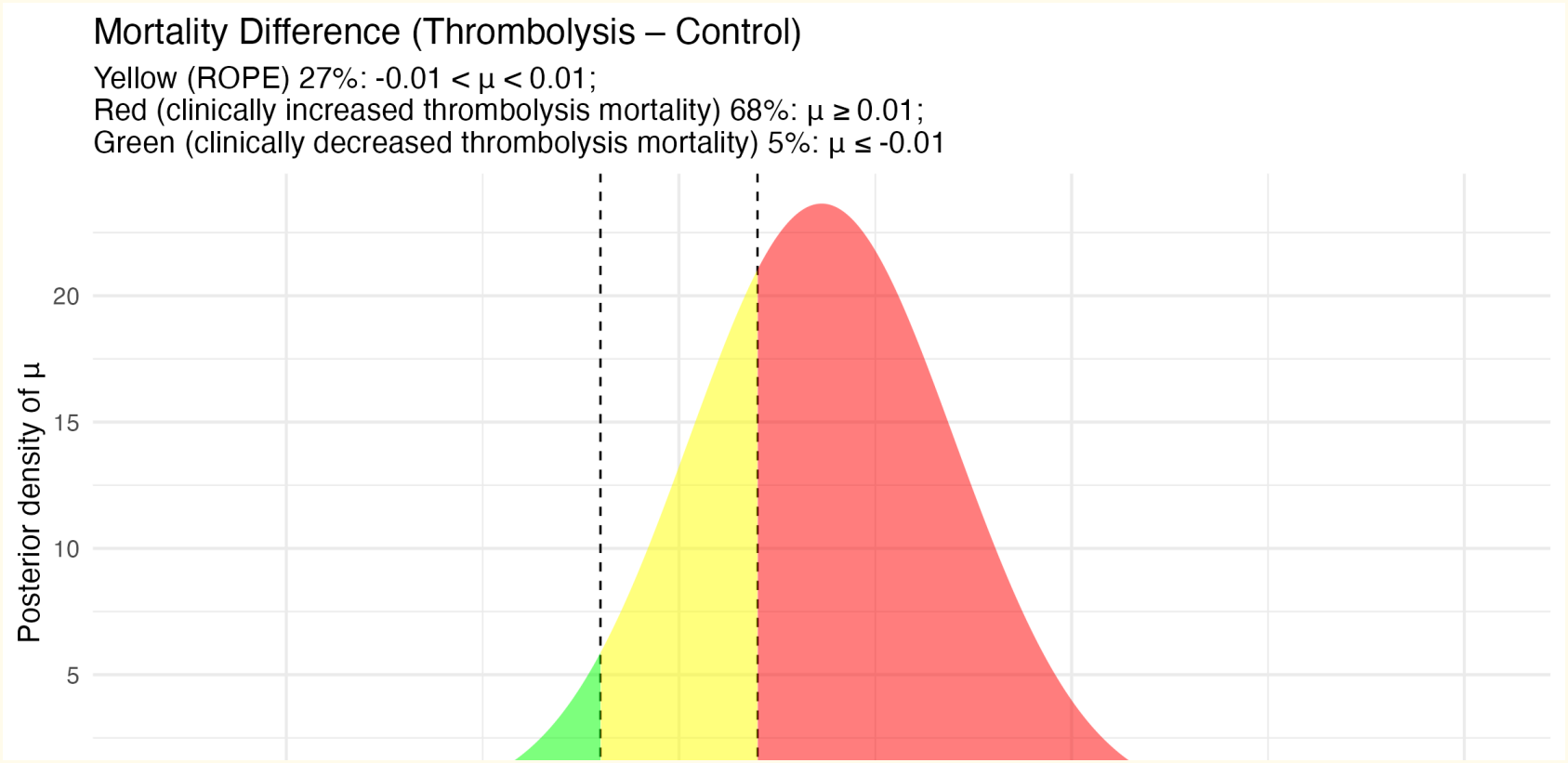
Probability mortality

RR > 1 = 76%

RR > 1.1 = 64%

Bayesian mortality (risk difference)

What is MCID for stroke mortality?
Assume MCID threshold = .01 (1%) as for MI



Summary extended thrombolysis

- Six recent RCTs of extended thrombolysis with guided advanced neuroimaging & seven MAs have been performed - all using dichotomized mRS outcome
- Bayesian MA of UW-mRS outcome shows a high probability of a difference in favor of thrombolysis but only a trivial probability of clinically meaningful benefit
- Bayesian MA shows a moderate probability of increased mortality
- Bayesian methods provide a richer, more interpretable analysis of clinical trial data

Dexmedetomidine (Precedex) & post-operative delirium (POD)

- Important to know if there are clinical advantages to offset the several fold higher costs compared to alternatives (placebo, opioid, or propofol)
- 14!!! prior meta-analyses majority suggested benefit but DECADE (largest RCT) ↑ POD
- Bayesian framework to:
  1. better propagation of uncertainties
  2. re-analyze DECADE under multiple priors
  3. build more complex models - quantify / adjust for possible (publication) bias 4) redo meta-analytic evidence with hierarchical model
  4. provide decision-relevant probabilities

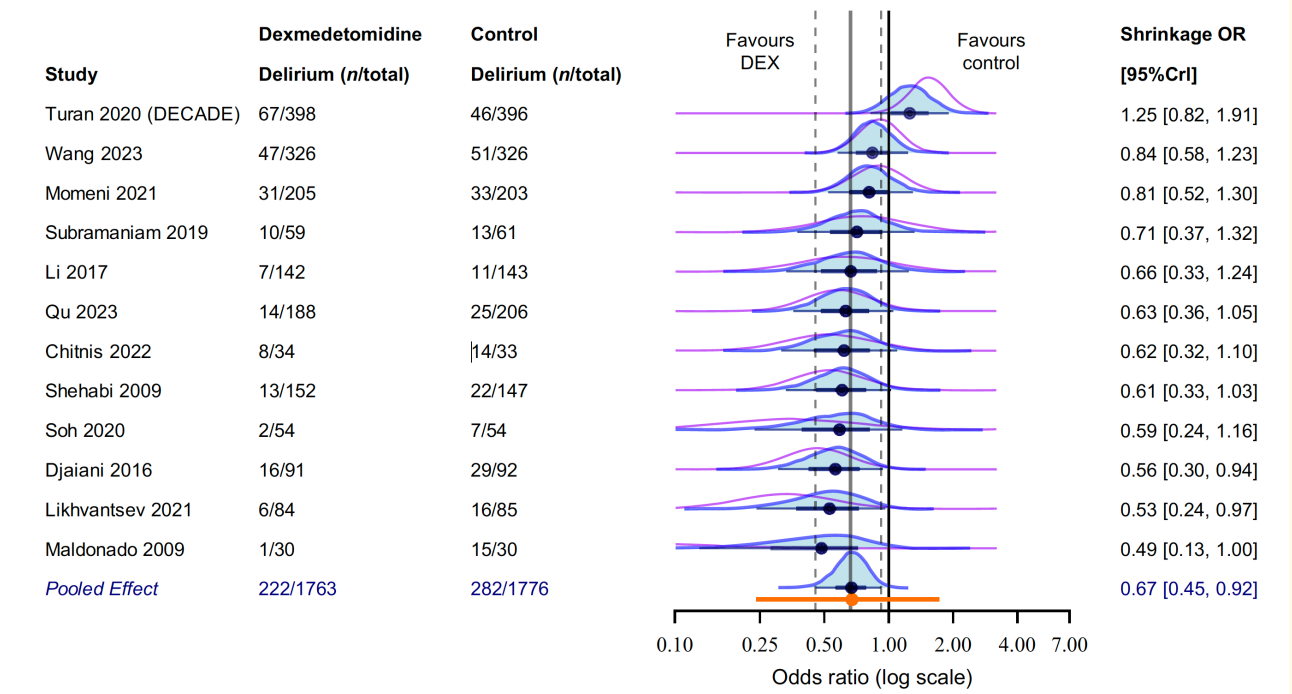
References:

1. Dexmedetomidine for Sedation in the ICU or PICU: A Review of Cost-Effectiveness and Guidelines [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2014 Dec 17. Available from: https://www.ncbi.nlm.nih.gov/books/NBK268693/

2. Turan A, Duncan A, Leung S, et al. Dexmedetomidine for reduction of atrial fibrillation and delirium after cardiac surgery (DECADE): a randomised placebo-controlled trial. Lancet 2020; 396: 177e85

Evidence & modeling choices

- 12 RCTs, 3,539 participants; primary outcome: incidence of POD
- Pooled OR 0.67 ([0.45, 0.92]), ↑ heterogeneity (control - placebo, opioid, or propofol)
  $\tau = 0.39\ [0.09, 0.75]$ → PI 0.24–1.78 (orange line)



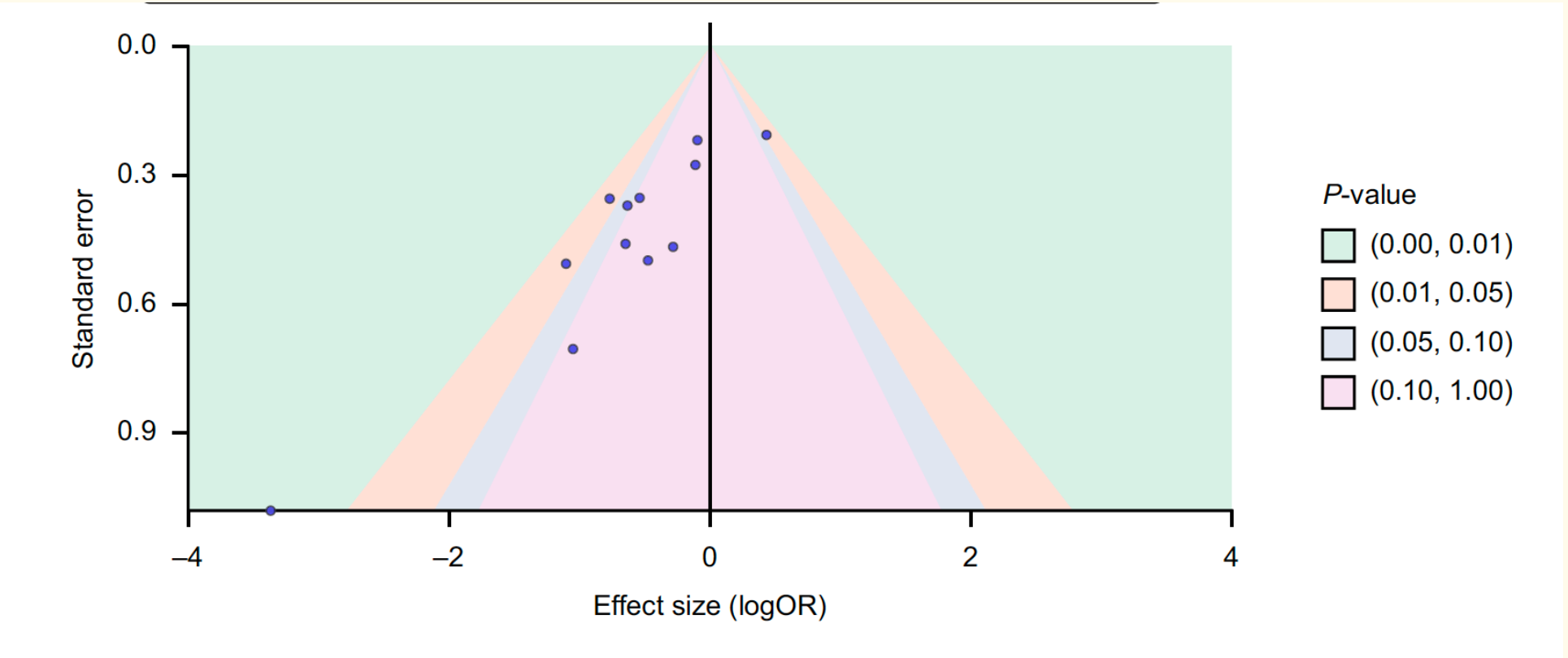
Model:

- Effect scale: log-OR; random-effects - normal–normal model

- Prior mean $\mu \sim \mathrm{N}(0, 0.82^2)$ -> 95% P (1/2.25 to 2.25), heterogeneity $\tau \sim \text{half-Cauchy}(0.5)$ (median 0.5, 95% < 2.5)

- MCID predefined (Cohen's d of >0.1) -> benefit OR < 0.84, harm OR > 1.20, ROPE 0.84 - 1.20

Publication bias: detect → adjust



- Bayesian funnel plot: strong asymmetry
  - regression slope $\beta \approx 3.86\ [2.41, 5.50]$ → small-study effects likely.
- Robust Bayesian Model Averaging (RoBMA) over selection models:
  - Inclusion $BF_{10} \approx 214$ for bias; mean-effect evidence attenuates $BF_{10} \approx 0.58$
- Very strong evidence for publication bias -> may ↓ effect size estimate

DECADE posterior distributions

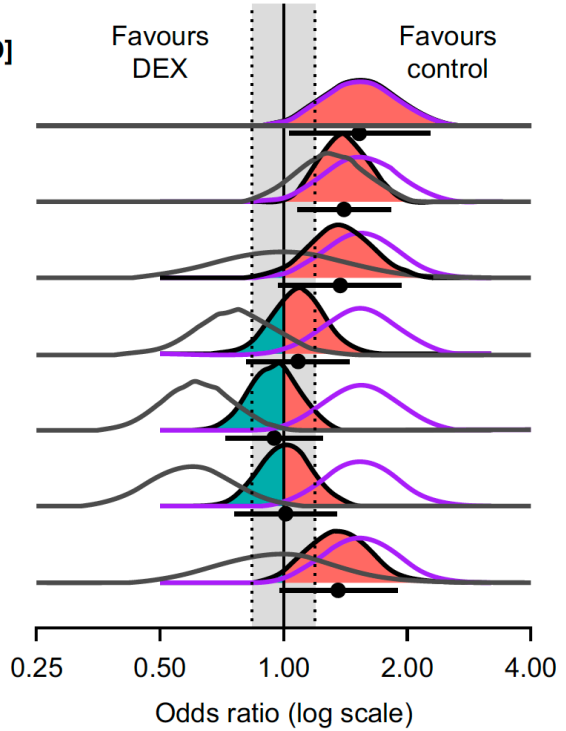
a

Prior information

Prior belief	Prior mean[SD]
Vague	1.00±10
Sceptical	1.31±0.19
Neutral	1.00±0.35
Optimistic	0.76+0.21
MA (all studies)	0.62±0.19
MA (low RoB)	0.60±0.23
MA (bias adj.)	0.97±0.32

b

Forest plot



c

Posterior probability of benefit/harm

Posterior 95%CrI	*P*(any benefit)	*P*(benefit >MCID)	P(any harm)	P(harm >MCID)
1.53 [1.03, 2.28]	1.5%	0.1%	98.5%	88.5%
1.40 [1.08, 1.84]	0.6%	0.0%	99.4%	87.9%
1.37 [0.97, 1.95]	3.8%	0.2%	96.2%	78.6%
1.09 [0.81, 1.45]	27.3%	3.6%	72.7%	25.2%
0.95 [0.72, 1.25]	63.7%	17.8%	36.3%	4.7%
1.01 [0.76, 1.35]	46.9%	9.8%	53.1%	12.7%
1.36 [0.98, 1.90]	3.4%	0.2%	96.6%	76.6%

- DECADE with vague prior: $P(\text{any benefit}) \approx 1.5\%$, $P(\text{benefit} \geq \text{MCID}) \approx 0.1\%$
- DECADE with unadjusted MA prior: $P(\text{benefit} \geq \text{MCID}) \approx 17.8\%$
- DECADE with bias-adjusted MA prior: $P(\text{benefit} \geq \text{MCID}) \approx 0.2\%$

Dexmedetomidine conclusions

- beware of individual RCT biases (late registration, early stopping, selective reporting)
- beware of meta-analytic biases (publication, selective inclusion)
- awareness is insufficient, need to try and model (quantify)
- final interpretations hinge on the prior & choice of MCID
- bias-aware priors align with no benefit / possible harm
- more research req'd to show any definitive benefit

Take-Home Messages

- Meta-analysis is powerful, but not infallible
- Bayesian meta-analysis:
  - ↑ flexibility
  - ↑transparency
  - ↑ acknowledgement & understanding of uncertainty
  - makes model assumptions explicit
  - respects the full evidence stream
  - avoids availability bias, dichotomous thinking
  - enhances clinical decision-making with relevant probabilities
    - *What's the probability RR < clinical meaningful effect?*
    - *What's the probability absolute benefit > clinical meaningful effect?*
  - ↑ meta-cognition -> ↑ better decisions via enhanced statistical reasoning

Thank You

Let's keep thinking critically, questions?

Slides available at https://www.brophyj.com/talks

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In memory of Dr. Maurice McGregor (1920 -2025)

mentor, colleague, friend, and critical thinker