Research Square

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A Bayesian probability-profile framework for meta-analysis: visualizing study-level heterogeneity and decision uncertainty Application to prone positioning during VV-ECMO for ARDS

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Abstract

Background: Conventional meta-analyses summarize heterogeneous evidence into a single pooled estimate, which can obscure how the strength of evidence varies across studies and what it implies for clinical decisions. Prone positioning during VV-ECMO for ARDS illustrates this problem: individual studies are inconsistent and frequentist meta-analyses are inconclusive. We introduce a Bayesian probability-profile framework that combines study-specific posterior probabilities, pooled estimates, likelihood ratios, and sensitivity analyses into a single interpretable output, and apply it to prone positioning during VV-ECMO for ARDS to quantify study-specific and pooled posterior probabilities of benefit on successful ECMO weaning and survival.

Methods: We conducted a secondary Bayesian reanalysis of aggregate data from eight published studies (2 RCTs, 6 observational; total n=1,046). Likelihood ratios were calculated based on minimal clinically important differences. Study-specific posterior probabilities Pr(RR > 1|data) were computed using vague priors, with sensitivity analyses across optimistic, skeptical, and historical priors, and after excluding the conference abstract (Martinez et al.). Pooled Bayesian random-effects meta-analyses were performed via PyMC in Python.

Results: The pooled posterior probability of benefit for successful ECMO weaning was 87% (median RR 1.17; 95% CrI, 0.83–1.51). For 28/30-day survival, the posterior probability was 82% (median RR 1.17; 95% CrI, 0.72–1.65). Study-specific analyses showed marked heterogeneity: four studies yielded >94% probability of benefit under vague priors, whereas two studies showed <35%. The largest RCT (PRONECMO) remained near equipoise (~50%). Subgroup analysis probabilities were higher in non-COVID-19 ARDS (98% for both weaning and survival) compared with COVID-19 ARDS (35% and 27%, respectively). Findings remained stable in direction across all sensitivity analyses.

Conclusions: A Bayesian probability-profile framework makes heterogeneity explicit and provides interpretive granularity beyond conventional pooling. Applied to prone positioning during VV-ECMO, it showed moderate-to-high aggregate probability of benefit with substantial variation across etiologies, supporting individualized decision-making and etiology-stratified randomized trials.

Background

Acute respiratory distress syndrome (ARDS) remains highly lethal even with lung-protective ventilation [1]. When hypoxemia is refractory, venovenous ECMO can rescue gas exchange and allow lung rest [2, 3], but hospital mortality among ECMO-supported patients still exceeds 40% in most series [4]. Identifying adjunctive therapies that could improve outcomes is therefore a research priority.

Prone positioning improves oxygenation, recruits dorsal lung units, and reduces mortality in ARDS patients who are not on ECMO [5, 6]. During VV-ECMO the same physiologic rationale holds—gravitational redistribution of perfusion, better ventilation-perfusion matching, improved secretion clearance [7, 8]. Yet the clinical evidence for a survival benefit in this setting remains inconclusive. Two meta-analyses since 2022 have examined prone positioning during VV-ECMO, and each has reported directionally favorable point estimates for survival [9, 10]. Both rely on frequentist null-hypothesis testing applied to fewer than 1,100 patients and moderate effect sizes. Under these constraints, conventional meta-analysis can suggest benefit without quantifying the residual uncertainty or its clinical implications [11].

Bayesian methods address this directly by estimating the probability—conditional on the observed data—that an intervention produces a clinically meaningful effect [12, 13]. In critical care, Bayesian reanalyses of frequentist-

neutral trials show that posterior probabilities favoring benefit are compatible with non-significant p-values [14, 15, 16]. Likelihood ratios provide a complementary, prior-free measure of evidence strength [17, 18]. These tools collectively generate what we term a "probability profile"—study-specific posterior probabilities alongside pooled estimates that highlights heterogeneity that conventional summaries conceal. They also facilitate systematic sensitivity analyses and formal publication bias assessment, both useful when the evidence base is small [19].

We therefore applied this framework to the published studies of prone positioning during VV-ECMO for ARDS, including the PRONECMO trial and Tong et al. [20, 21]. Our objectives were to characterize how evidence strength was distributed across studies; to test whether pooled estimates withstood pre-specified sensitivity analyses; to evaluate the framework's operating characteristics in a simulation study; to evaluate publication bias using Egger's regression and funnel plot inspection (see Additional file 1); and to present the results as a probability profile that informs clinical decision-making more directly than a single pooled risk ratio.

Methods

Study Selection and Data Extraction

We performed a secondary Bayesian reanalysis of aggregate data from previously published studies. The eight eligible studies (2 randomized controlled trials and 6 observational studies, totaling 1,046 patients) were drawn from the most recent systematic reviews and meta-analyses [22] covering prone positioning during VV-ECMO for ARDS up to 2025. No new systematic literature search was performed for this reanalysis. This secondary Bayesian reanalysis and data synthesis followed the PRISMA 2020 reporting guideline where applicable. Individual observational studies were evaluated according to the STROBE reporting guidelines. Study characteristics, risk ratios (RRs), confidence intervals, and event rates for successful ECMO weaning and survival outcomes were extracted as originally reported. Risk of bias was appraised with ROBINS-I [23] for observational studies and RoB 2 [24] for RCTs. Full risk-of-bias ratings appear in Additional file 1.

Likelihood Ratio Analysis

Likelihood ratios (LRs) were calculated to quantify the strength of evidence for a clinically meaningful benefit of prone positioning versus no benefit, following the methodology of Perneger and Gayet-Ageron [17]. Calculations were based on the minimal clinically important differences (MCIDs) for risk ratios proposed by Guervilly et al.: RR = 1.39 for successful ECMO weaning and RR = 1.55 for 28/30-day survival [25]. These MCID thresholds were derived from expert consensus on prone positioning during VV-ECMO and represent a relative risk increase deemed clinically meaningful by clinicians caring for these patients [25]. For studies reporting zero events in a cell, a 0.5 continuity correction was applied. Evidence strength was interpreted as follows: LR 1–3 weak, 3–10 moderate, 10–30 substantial, 30–100 strong, 100–300 very strong, and >300 decisive.

Bayesian Posterior Probability Analyses

Both study-specific and pooled Bayesian analyses were performed. Study-specific analyses were conducted independently for each study [15]. For study-specific analyses, posterior probabilities of benefit $Pr(RR > 1 \mid data)$ were calculated for each study and each outcome. Our primary analysis used vague (near-non-informative) priors centered at zero on the log-RR scale ($\mu \sim Normal[0, 10^2]$), reflecting clinical equipoise with wide variance. Sensitivity analyses were conducted using optimistic ($\mu \sim Normal[0.2, 0.15^2]$), skeptical ($\mu \sim Normal[0, 0.1^2]$), and historical priors informed by Guervilly et al. [25]. For heterogeneity (τ), we used a half-Normal(0, 1) prior to allow for a plausible range of between-study variability while providing weak regularization. For pooled analyses, Bayesian random-

effects meta-analyses were performed using PyMC in Python. Risk ratios were modeled on the log scale with a Gaussian family and a random intercept for study. Between-study heterogeneity τ was quantified as the standard deviation of the random effects. Posterior sampling relied on Markov chain Monte Carlo with 4 chains, 12,000 iterations per chain (3,000 discarded as warmup). Convergence was checked with R-hat < 1.01 and effective sample size (ESS) > 400. Publication bias was screened graphically with funnel plots of the log risk ratio against its standard error and formally tested with Egger's regression. For the primary survival analysis, one endpoint per study was selected prioritizing 28- or 30-day survival when available, followed by 60-day and 90-day survival. Pre-specified sensitivity analyses included different prior distributions, pooling of all available survival time points, restriction to randomized controlled trials only, and exclusion of the Garcia et al. study as an outlier. Subgroup analyses stratified studies by ARDS etiology (COVID-19 versus non-COVID-19). All analyses and visualizations were performed in Python with PyMC. The statistical code is provided as Additional file 2.

Simulation Study

To evaluate the operating characteristics of the probability-profile framework, we conducted a simulation study mirroring realistic conditions for small meta-analyses in critical care. Six scenarios were simulated (500 replicates each), crossing the true effect size (RR 1.0 to 1.5) with between-study heterogeneity (τ 0.0 to 0.5), representing null, small, moderate, and large benefit scenarios. For each replicate, Bayesian posterior probabilities of benefit were computed analytically from summary data using conjugate normal models (without MCMC sampling), and frequentist p-values were obtained from standard random-effects meta-analysis. Detection rates were defined as the proportion of replicates achieving frequentist significance ($p < 0.05$) versus Bayesian strong evidence ($Pr > 0.95$). Simulation results are presented in the Results section.

Results

Study Characteristics and Likelihood Ratios

Eight previously published studies (2 RCTs, 6 observational; total n = 1,046) were eligible for reanalysis. These comprised two prospective multicenter RCTs (PRONECMO [20], Tong et al. [21]), one prospective observational study [30], and five retrospective observational studies [26,27,28,29,31] conducted in France, China, Germany, and Spain. Table 1 summarizes study characteristics and outcomes. Likelihood ratios for a clinically meaningful benefit of prone positioning varied widely, from 0.06 to 29.59 for successful ECMO weaning and from 0.00 to 17.32 for survival outcomes. LR exceeded 10 in Petit et al. (LR 15.33 for weaning; 17.32 for survival) and Tong et al. (LR 29.59 for weaning), and approached this threshold in Tang et al. (LR 7.33–7.89), whereas Garcia et al. and Martinez et al. (conference abstract) provided strong or very strong evidence against benefit (Figure 1).

Pooled Bayesian Meta-Analysis

For the primary analysis with vague priors, the posterior median risk ratio for successful ECMO weaning was 1.17 (95% CrI 0.83–1.51), corresponding to an 87% posterior probability of benefit (τ = 0.26; 95% CrI, 0.01–0.82) (Table 2). For 28/30-day survival, the posterior median risk ratio was 1.17 (95% CrI 0.72–1.65), with an 82% posterior probability of benefit. When all available survival time points were pooled, the posterior probability remained 82%. Restriction to the two RCTs alone substantially widened the credible intervals (weaning: median RR 1.25, 95% CrI 0.45–3.69) and lowered the posterior probability to 76% for weaning and 67% for survival. The very wide CrI reflects the substantial uncertainty when only two RCTs are available. Exclusion of Garcia et al. increased the probability to 96% for weaning and 95% for survival (Table 2).

Study-Specific Bayesian Posterior Probabilities

Study-specific analyses showed substantial heterogeneity in the strength of evidence (Table 3; Figure 2). Using vague priors, four studies showed posterior probabilities of benefit above 94%: Tong et al. (99.6% for weaning; 98.1% for survival), Petit et al. (98.9% for weaning; 99.5% for survival), Tang et al. (97.7% for both), and Chen et al. (94.8% for weaning). In contrast, Garcia et al. (1.2% for both) and Martinez et al. (conference abstract; 19.8% for weaning) yielded very low probabilities. The PRONECMO trial (Schmidt et al.) produced probabilities near 50%, indicating clinical equipoise. Rilinger et al. showed intermediate probabilities (52.6% for weaning; 82.1% for survival).

Simulation Results

Across all six scenarios, Bayesian detection rates exceeded frequentist detection rates, with the largest advantage under moderate heterogeneity ($\tau = 0.3$) and smaller effect sizes, where frequentist tests have limited power (Figure 3, panel A). The trade-off between type I error control and statistical power favored the Bayesian approach in the small-sample settings typical of critical care meta-analyses (Figure 3, panel B).

Sensitivity and Subgroup Analyses

Pre-specified sensitivity analyses reproduced the primary findings (Table 2; see Additional file 1). Across skeptical, optimistic, and historical priors, the pooled probability of benefit for ECMO weaning fell between 77% and 97%. Probabilities of benefit were higher in non-COVID-19 ARDS (98% for weaning; 98% for survival) compared with COVID-19 ARDS (35% and 27%, respectively). The divergence between etiologies persisted across all sensitivity analyses.

Discussion

These eight studies, totaling 1,046 patients, represent the entire published evidence base for prone positioning during VV-ECMO. Reanalyzing these data from a Bayesian standpoint gives a posterior probability of benefit of 87% for successful ECMO weaning (median RR 1.17; 95% CrI, 0.83–1.51) and 82% for 28/30-day survival (median RR 1.17; 95% CrI, 0.72–1.65). Under our chosen prior specification, these numbers correspond to roughly 7:1 and 5:1 odds of benefit, respectively. What this analysis adds beyond previous meta-analyses [9,10] is not a new point estimate—our summary risk ratios are consistent with theirs—but a quantification of what the evidence implies for clinical decisions. A frequentist meta-analysis of the same data would report non-significant p-values (the 95% CI crosses 1.0) and might be interpreted as showing "no effect." The Bayesian results show otherwise: the evidence supports benefit, but with uncertainty that should inform—not end—the discussion.

The study-specific probabilities tell a different story than the pooled estimates alone (Table 3; Figure 2). In four studies (Tong et al., Petit et al., Tang et al., and Chen et al.), the weaning posterior probability exceeded 94%, pointing to strong evidence of benefit in those settings. At the other extreme, Garcia et al. (1.2%) and Martinez et al. (19.8%) provided evidence against benefit. The PRONECMO trial, the largest and methodologically strongest study, produced a posterior probability of ~50%—essentially equipoise. This bimodal distribution likely reflects differences in study design, population, and era. PRONECMO was a randomized trial restricted to COVID-19 patients; Tong and Petit included predominantly non-COVID ARDS; Garcia enrolled exclusively COVID-19 patients in the early pandemic wave. Presenting these as a "probability profile" makes visible what a pooled estimate inevitably conceals: the evidence points in opposite directions for different patient subgroups.

Subgroup analysis by ARDS etiology confirmed this pattern. In non-COVID-19 ARDS [32], the posterior probability of benefit was approximately 98% for both weaning and survival; among COVID-19 patients, it was 35% and 27%, respectively. This disparity persisted across all prior specifications and sensitivity analyses. These findings are consistent with established pathophysiology. COVID-19-associated ARDS is characterized by endothelial injury, microvascular thrombosis, and relatively homogeneous lung involvement—features that may limit the positional recruitment that proning exploits.

The 87% pooled estimate is sensitive to a single outlier: removing Garcia et al. (the only strongly negative study) shifts the weaning probability to 96%. Under skeptical priors, it drops to 77%. Restricting the analysis to the two RCTs alone produces enormous uncertainty (CrI 0.45–3.69 for weaning), confirming that randomized evidence—only 270 patients—cannot bear the weight of meta-analytic inference. Publication bias merits consideration. For weaning, Egger's test found no statistically significant funnel asymmetry (weaning: $p = 0.13$; survival: $p = 0.29$), although the funnel plots visually suggest a shortage of moderate-sized null studies, a pattern consistent with small-study effects (see Additional file 1). This pattern would be expected under selective non-publication of negative results, which would inflate the pooled probability. With only eight studies, funnel-plot diagnostics have limited power, but the possibility that the published literature overstates the benefit of proning during ECMO is real.

Should these results change practice? An 87% posterior probability corresponds to roughly 7:1 odds of benefit—a level many clinicians would accept for a low-risk maneuver. But relying on this single number would be misleading. For a non-COVID-19 ARDS patient in an experienced center, the probability of benefit may approach 98%; for a COVID-19 patient it may fall below 40%. Clinicians relying solely on the pooled estimate would overlook this distinction. Equally important is how little it takes to perturb the pooled result. Excluding a single small study shifts the probability from 87% to 96%; adopting a skeptical prior drops it to 77%. The positive signal rests largely on observational data, and the funnel plot asymmetry raises legitimate concerns about selective reporting. Prone positioning during VV-ECMO remains physiologically plausible, carries relatively low risk, and may benefit selected patients—particularly those with non-COVID etiology. But the evidence as it stands does not support a standard-of-care recommendation.

This analysis has several limitations. It is a secondary reanalysis of published aggregate data rather than a de novo systematic review, so eligible studies may have been missed. Six of the eight included studies are observational, and confounding by indication—sicker patients being less likely to be proned—cannot be excluded. The evidence base is modest (1,046 patients), and the wide credible intervals across most comparisons reflect genuine statistical uncertainty. Individual patient data were not available, precluding detailed confounder adjustment or patient-level subgroup analyses; the substantial group imbalance in the Rilinger et al. cohort (38 prone vs. 120 control) reflects non-randomised treatment assignment and may introduce residual confounding despite our hierarchical Bayesian approach. One of the eight studies (Martinez et al.) has only been published as a conference abstract without full peer review, and the MCID thresholds used for the LR analysis rest on expert consensus rather than anchor-based or distribution-based derivation. Funnel plot asymmetry raises the possibility of publication bias, which would tend to overestimate benefit, although Egger's test may have limited power to detect asymmetry with fewer than 10 studies. With only eight studies, the between-study variance (tau) was also imprecisely estimated (95% CrI 0.01-0.82 for weaning), and pooled estimates should be interpreted in light of this uncertainty. The included studies also varied in proning protocols, session duration, timing of initiation, and weaning criteria, limiting cross-study comparability.

The available data suggest that prone positioning during VV-ECMO is more likely than not to improve outcomes, especially for weaning and in non-COVID-19 ARDS. But "more likely than not" is a long way from "proven." The evidence is fragile, heterogeneous, and potentially biased by selective reporting (see Additional file 1). A properly

powered, etiology-stratified randomized trial with standardized proning protocols and patient-centered endpoints is needed to resolve this question. Until such data exist, prone positioning during VV-ECMO should be regarded as a reasonable, individualized clinical decision rather than a standard of care.

Conclusions

Bayesian analysis of the evidence for prone positioning during VV-ECMO shows moderate-to-high probability of benefit in the aggregate, with substantial variation across patient subgroups and study designs. The pooled estimate masks a bimodal distribution of study-level effects better explained by differences in ARDS etiology than by chance. These findings do not support a uniform approach; they favor individualized decision-making. A definitive answer requires randomized evidence adequately powered and stratified by ARDS phenotype.

Abbreviations

ARDS = acute respiratory distress syndrome

CrI = credible interval

ECMO = extracorporeal membrane oxygenation

LR = likelihood ratio

MCMC = Markov chain Monte Carlo

MCID = minimal clinically important difference

PP = prone positioning

RCT = randomized controlled trial

RR = risk ratio

VV-ECMO = venovenous extracorporeal membrane oxygenation

Pr(RR > 1) = posterior probability of risk ratio greater than 1

ROBINS-I = Risk Of Bias In Non-randomised Studies - of Interventions

RoB 2 = Revised Cochrane Risk of Bias Tool for Randomized Trials

Declarations

Ethics approval and consent to participate

Because this work is a secondary Bayesian reanalysis of published, aggregate, de-identified data, ethics committee approval was not required under institutional policy.

Clinical trial number

Clinical trial number: not applicable.

Consent for publication

Not applicable.

Availability of data and materials

All data analysed during this study are derived from the published articles cited in the references. The datasets analysed are available from these publications. The statistical code supporting the conclusions of this article is provided as Additional file 2.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

XY: Conceptualization, Data curation, Formal analysis, Methodology, Writing – original draft. WZ: Conceptualization, Investigation, Methodology, Validation, Writing – review & editing. JP: Conceptualization, Methodology, Supervision, Project administration, Writing – review & editing. All authors approved the final manuscript and agree to be accountable for all aspects of the work.

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Use of artificial intelligence

During the preparation of this work, the authors used AI-assisted language editing tools for proofreading and polishing the manuscript. After using these tools, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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Tables

Table 1. Characteristics and Outcomes of Included Studies

Study	Design	Country	Primary Etiology	N (Prone/Control)	ECMO Weaning*	28/30d Survival*	RoB
Schmidt 2023 (PRONECMO)	RCT	France	Mixed	86/84	38/37	46/49 (60d)	Low
Tong 2024	RCT	China	Mixed	49/48	38/24	33/22 (30d)	Low
Rilinger 2020	Retrospective cohort	Germany	Mixed	38/120	18/56	18/47 (30d)	Moderate
Garcia 2020	Retrospective cohort	France	COVID-19	14/11	3/8	3/8 (28d)	Serious
Chen 2022	Retrospective cohort	China	Mixed	25/25	14/8	N/R	Moderate
Petit 2022	Retrospective cohort	France	Mixed	64/64	48/35	51/37 (90d)	Moderate
Tang X 2024	Prospective cohort	China	Mixed	45/45	29/19	28/18 (60d)	Moderate
Martinez 2021	Retrospective cohort	Spain	COVID-19	43/285	17/134	N/R	Moderate

** Values are events/total for prone vs control arms. N/R = not reported in primary study for this outcome.*

Table 2. Pooled Bayesian Posterior Probability Results

Analysis	Median RR	95% CrI	P(RR > 1)	Median τ	95% CrI for τ
Primary Weaning	1.17	0.83–1.51	0.87	0.26	0.01–0.82
Primary Survival (1 endpoint/study)	1.17	0.72–1.65	0.82	0.29	0.03–0.98
RCTs Only – Weaning	1.25	0.45–3.69	0.76	0.46	0.03–1.97
RCTs Only – Survival	1.14	0.37–3.93	0.67	0.49	0.03–1.96
Exclude Garcia – Weaning	1.23	0.97–1.56	0.96	0.19	0.01–0.62
Exclude Garcia – Survival	1.25	0.91–1.72	0.95	0.20	0.01–0.79
COVID-19 Weaning	0.92	0.44–1.62	0.35	0.37	0.02–1.56
COVID-19 Survival	0.84	0.30–1.93	0.27	0.47	0.02–1.39
Non-COVID Weaning	1.39	1.04–1.93	0.98	0.16	0.01–0.67
Non-COVID Survival	1.43	1.03–2.04	0.98	0.14	0.01–0.72
COVID-19 subgroup: Garcia et al. (2020) and Martinez et al. (2021). Non-COVID-19 subgroup: Schmidt et al. (2023), Tong et al. (2024), Rilinger et al. (2020), Chen et al. (2022), Petit et al. (2022), and Tang et al. (2024).					

Table 3. Study-Specific Posterior Probabilities (Vague Priors)

Study	Outcome	Median RR	95% CrI	P(RR > 1)	Strength of Evidence
Schmidt	ECMO weaning	1.00	0.72–1.40	50.1%	Equipoise
Schmidt	60-day survival	0.92	0.75–1.13	21.8%	Very low
Tong	ECMO weaning	1.55	1.12–2.15	99.6%	Very strong
Tong	30-day survival	1.47	1.02–2.14	98.1%	Very strong
Rilinger	ECMO weaning	1.01	0.68–1.49	52.6%	Equipoise
Rilinger	30-day survival	1.21	0.80–1.82	82.1%	Moderate
Garcia	ECMO weaning	0.30	0.10–0.86	1.2%	Very low
Garcia	28-day survival	0.30	0.10–0.86	1.2%	Very low
Chen	ECMO weaning	1.75	0.88–3.46	94.8%	Strong
Petit	ECMO weaning	1.37	1.05–1.79	98.9%	Very strong
Petit	90-day survival	1.38	1.08–1.76	99.5%	Very strong
Tang X	ECMO weaning	1.56	1.01–2.39	97.7%	Very strong
Tang X	60-day survival	1.56	1.01–2.39	97.7%	Very strong
Martinez	ECMO weaning	0.84	0.57–1.25	19.8%	Very low

Figures

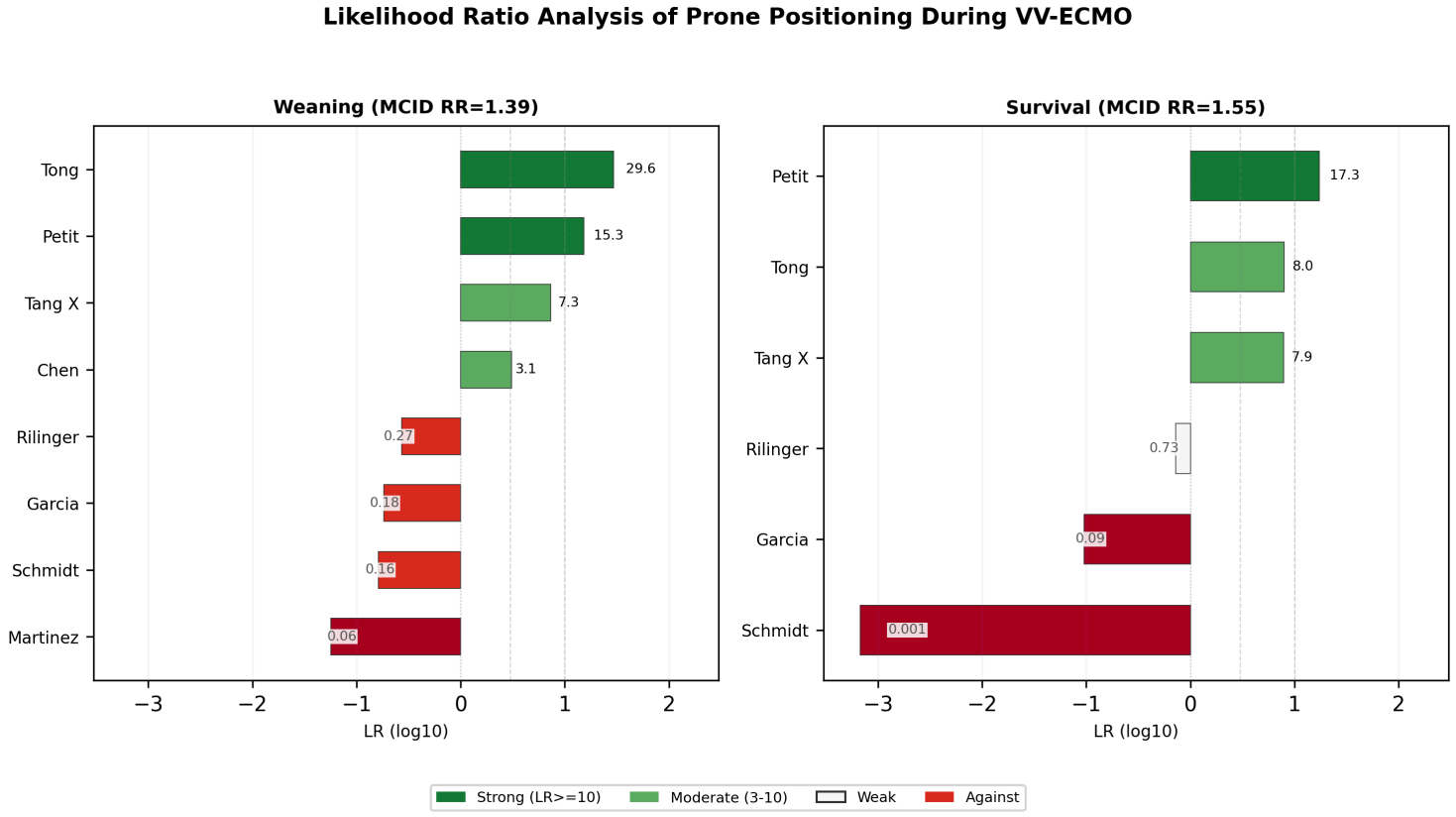


Figure 1

Likelihood Ratios for Prone Positioning Effects on Successful ECMO Weaning and Survival. LRs across eight included studies. Circle size proportional to sample size; circles represent RCTs; triangles represent observational studies. Dashed line = LR = 1.

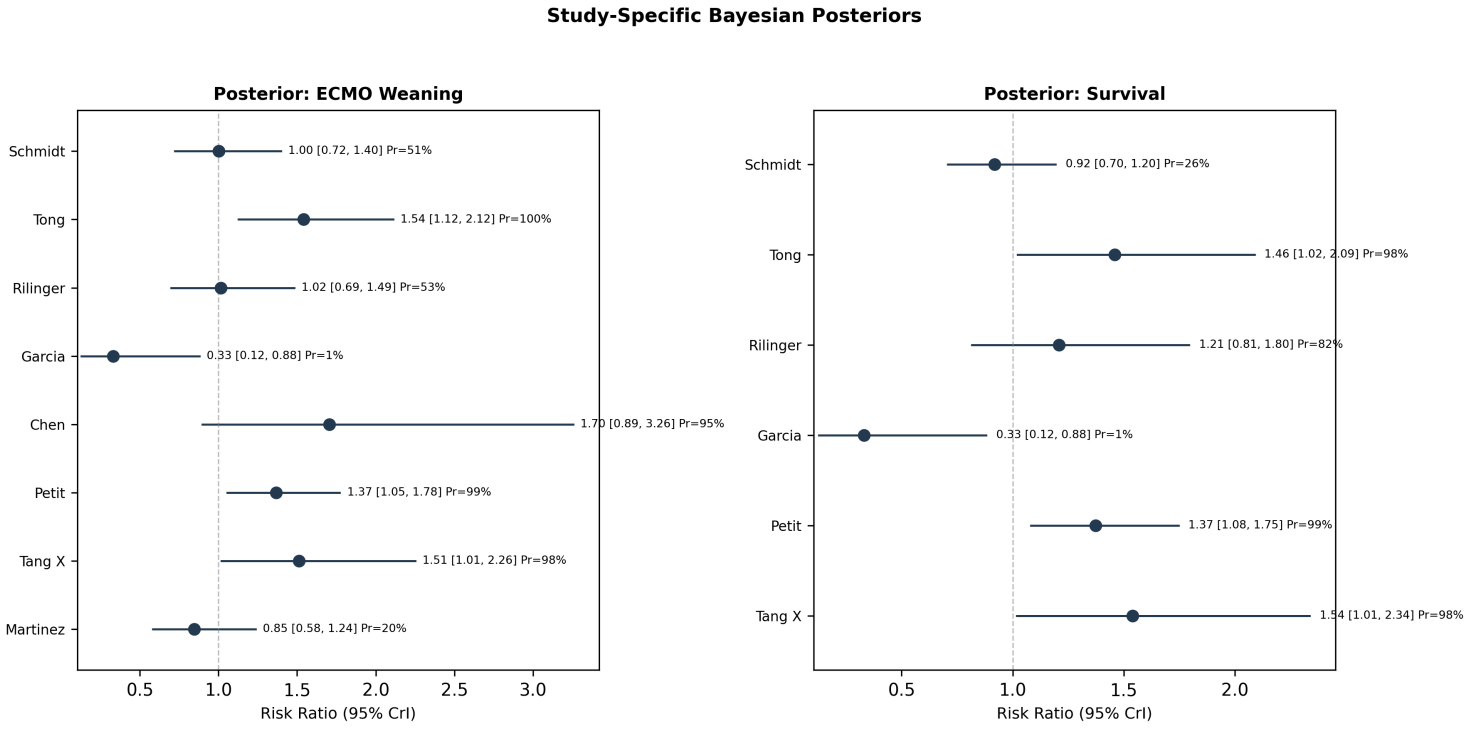


Figure 2

Study-Specific Posterior Probabilities of Benefit. Pr(RR > 1 | data) under vague priors. Dark blue: ≥90% (strong benefit), light blue: 70–89% (moderate), gray: 40–69% (equipoise), red: <30% (evidence against benefit).

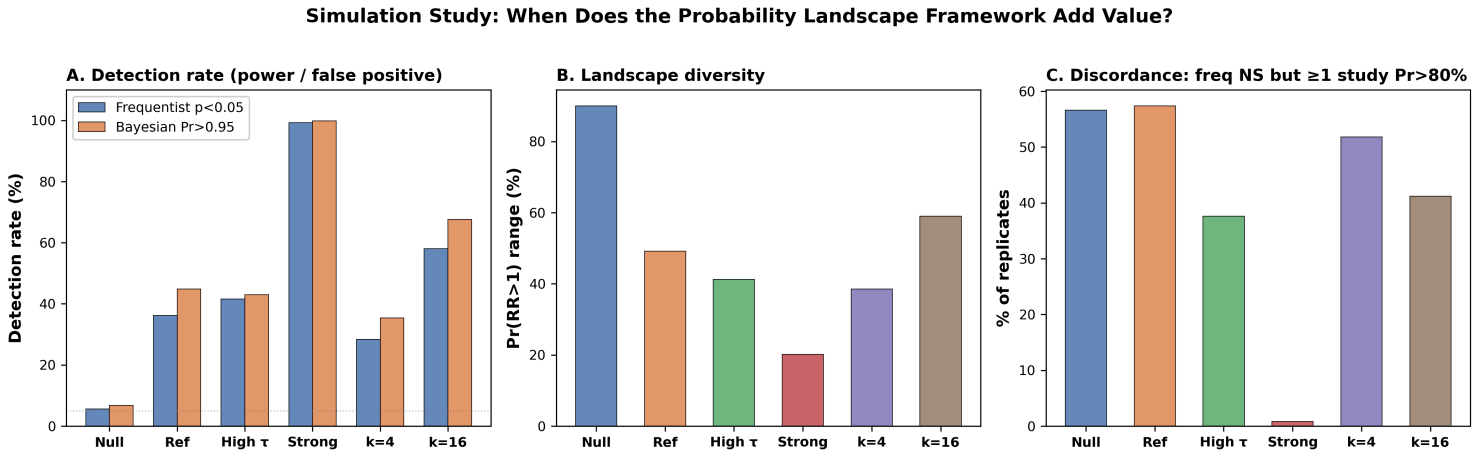


Figure 3

Simulation Results. (A) Detection rates of Bayesian strong evidence (Pr > 0.95) versus frequentist significance (p < 0.05) across six scenarios (500 replicates each) spanning true RR 1.0–1.5 and τ 0.0–0.5. (B) Trade-off between type I error and statistical power, showing the advantage of the Bayesian approach in small-sample meta-analyses.

Supplementary Files

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- Additionalfile1eSupplement.docx