Crimi *et al. J Anesth Analg Crit Care* (2026) 6:52
https://doi.org/10.1186/s44158-026-00361-3

Journal of Anesthesia, Analgesia and Critical Care

RESEARCH

Open Access

High-flow nasal therapy vs conventional oxygen therapy in mild COVID-19 hypoxaemia: a Bayesian reanalysis of the COVID-HIGH Trial

Claudia Crimi[1,2†], Salvatore Sardo[3†], Alberto Noto[4], Fabiana Madotto[5], Mariachiara Ippolito[6,7], Santi Nolasco[2], Raffaele Campisi[2], Giuseppe Fiorentino[8], Ioannis Pantazopoulos[9], Athanasios Chalkias[10,11,12], Alessio Mattei[13], Raffaele Scala[14], Enrico Clini[15], Begum Ergan[16], Manel Lujan[17], João Carlos Winck[18,19], Antonino Giarratano[6,7], Annalisa Carlucci[20,21], Cesare Gregoretti[22,23], Paolo Groff[24], Andrea Cortegiani[6,7*] and COVID-HIGH Investigators

Abstract

Background Clinical effectiveness of high-flow nasal therapy (HFNT) over conventional oxygen therapy (COT) in patients with mild COVID-19-related acute hypoxaemic respiratory failure (AHRF) remains uncertain. The COVID-HIGH trial did not demonstrate statistically significant benefits of HFNT over COT. However, the trial was slightly underpowered, and the event rate lower-than-expected. Bayesian methods provide deeper insight by incorporating prior knowledge and quantifying uncertainty intuitively. This analysis aimed to quantify the probability of benefit or harm associated with HFNT, adopting a Bayesian approach.

Methods We performed a Bayesian reanalysis of the COVID-HIGH trial (NCT, which randomised 364 patients with PaO_2/FiO_2 between 200–300 mmHg to receive HFNT or COT. The primary outcome was escalation of respiratory support (continuous positive airway pressure, noninvasive ventilation or invasive mechanical ventilation) within 28 days. A key secondary outcome was clinical recovery at day 14. Bayesian logistic models with noninformative and informative priors were used to estimate the posterior probability of treatment effects.

Results Escalation of respiratory support occurred in 23.6% (HFNT) versus 30.2% (COT) (risk difference − 6.6%, 95% CI − 15.1 to 2.1; p = 0.14). Across a wide range of priors, the posterior probability mass on the beneficial side remained high, generally > 70%, while the proportion on the harm side remained consistently low at ≤ 6% for all models, underscoring a favourable benefit-risk profile. The acute respiratory failure meta-analysis model (OR 0.76, 95% CrI 0.60—0.97), the COVID-19 randomised evidence model (OR 0.76, 95% CrI 0.60—0.97), the COVID-19 observational evidence model (OR 0.60, 95% CrI 0.45—0.80), and the COVID-19 Bayesian meta-analysis mixed evidence model (OR 0.66, 95% CrI 0.52—0.86) showed posterior probability mass on the beneficial side of 70%—94%. Clinical recovery at day 14 occurred in 61.5% (HFNT) versus 53.3% (COT), with 61–73% of posterior probability mass on the clinical benefit side.

†Claudia Crimi and Salvatore Sardo are co-first authors.

*Correspondence:
Andrea Cortegiani
andrea.cortegiani@unipa.it
Full list of author information is available at the end of the article

Conclusions This Bayesian re-analysis of the COVID-HIGH trial suggests that HFNT likely reduces escalation of respiratory support and improves clinical recovery in patients with COVID-19 pneumonia and mild hypoxaemia, although the magnitude of benefit remains uncertain and sensitive to prior assumptions.

Trial registration The trial was prospectively registered in ClinicalTrials.gov on December 7, 2020 (NCT04655638).

Keywords High-flow nasal therapy, Acute hypoxemic respiratory failure, Mild hypoxemia, COVID-19 pneumonia, Bayesian statistics

Introduction

Acute hypoxaemic respiratory failure (AHRF) is a frequent and life-threatening manifestation of COVID-19, often requiring escalation from conventional oxygen therapy (COT) to advanced respiratory support, including high-flow nasal therapy (HFNT), continuous positive airway pressure (CPAP), noninvasive ventilation (NIV) or invasive mechanical ventilation (IMV). While HFNT has demonstrated efficacy in reducing intubation rates and improving clinical outcomes in patients with moderate-to-severe AHRF of non-COVID aetiology, evidence supporting its benefit in patients with mild hypoxaemia due to COVID-19 remains limited and uncertain [1–7].

The COVID-HIGH trial was the first large multicentre randomised controlled trial (RCT) specifically designed to evaluate whether HFNT, compared with COT, reduces the risk of escalation of respiratory support in patients with COVID-19 and mild hypoxaemia [7, 8]. Although COVID-HIGH did not demonstrate a statistically significant difference in its primary outcome, frequentist analysis may not fully capture the uncertainty surrounding treatment effects, especially in trials with modest event rates or potential for type II error. Indeed, the trial was underpowered for the primary outcome due to a pre-planned sample size calculation based on available data at the beginning of the pandemic [9].

Bayesian methods offer an alternative framework that incorporates prior knowledge and directly quantifies the probability of clinically important benefits or harms, thus providing a more nuanced interpretation of trial results [10]. Recent studies have demonstrated how Bayesian re-analyses can recontextualise findings from large RCTs by integrating external evidence or exploring the impact of different prior assumptions on the estimated treatment effects.

Therefore, we performed a Bayesian re-analysis of the COVID-HIGH trial to estimate the probability that HFNT reduces the risk of escalation of respiratory support or influences other clinically relevant outcomes. This re-analysis aims to complement the original frequentist results by offering a probabilistic interpretation of HFNT's potential benefits or harms in patients with COVID-19 and mild hypoxemia, which may guide clinicians in selecting appropriate respiratory support strategies in this population.

Methods

We reanalysed data from the COVID-HIGH trial, which enrolled 364 adult patients (≥ 18 years) with confirmed COVID-19 pneumonia and mild hypoxaemic respiratory failure, defined as PaO_2/FiO_2 between 200–300 mmHg. Patients were randomised to receive either HFNT or COT. Full details on trial design and patient characteristics are available in the original COVID-HIGH trial primary results manuscript (Trial registration number NCT04655638) [8].

We conducted Bayesian analyses following the framework outlined by Zampieri et al., employing generalised linear models to evaluate the effect of the intervention—HFNT versus COT—on both the primary and one selected secondary outcome [10].

The primary outcome was defined as the proportion of patients requiring escalation of respiratory treatment, i.e., CPAP, NIV, or IMV, within 28 days. The secondary outcome chosen for Bayesian analysis was the proportion of patients who terminated the study protocols due to improvement (clinical recovery, defined as the improvement in oxygenation with the ability to maintain $SpO_2 \geq 96\%$ with $FiO_2 \leq 30\%$ or PaO_2/FiO_2 ratio > 300 mmHg). Patients and public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

The trial was prospectively registered in ClinicalTrial.gov on December 7, 2020 (NCT04655638). The study protocol of the original COVID-HIGH trial was approved by the Ethics Committee of the coordinating centre (Comitato Etico Catania 1, 01/2021/PO, 25/01/2021) and all participating sites before patient inclusion. The study was performed in accordance with Good Clinical Practice guidelines and ethical principles of the Declaration of Helsinki. The trial was overseen by an oversight committee comprised of independent clinicians with no competing interests. Written informed consent was obtained from all patients or surrogates.

Model structure and prior specification

We implemented the regression models using the brms package (version 2.22.0) in the R statistical computing environment (R version 4.5.1, R Core team, 2023), interfacing with the Stan probabilistic programming language [11–15]. For each outcome, we fitted a Bayesian model using the Beta-Bernoulli conjugate framework to estimate the outcome probabilities in each group, using priors that reflected different levels of prior belief strength, including sceptical, optimistic, and flat specifications. We did not include clinical or enrolment site covariates in our linear models (see Supplementary Material for an example of brms model). Prior distributions were defined as Normal distributions on the natural log-odds ratio (log(OR)) scale. The mean of the distribution represented the expected treatment effect, while the standard deviation (SD) encoded the strength of belief in that effect: smaller SDs indicated stronger prior certainty. Specifically, we defined four levels of prior informativeness: strong prior (SD = 0.1), moderately strong or intermediate prior (SD = 0.4), weak prior (SD = 0.8), and flat non-informative prior (SD = 1000).

The clinical translation of the priors based on Cohen's effect sizes for the primary outcome, escalation of respiratory support, assumes a control event rate of 38.6%. Under this baseline risk, a small effect size corresponds to an absolute change of approximately 9 to 10 events per 100 patients, either as a reduction or an increase in escalation rates. A moderate effect size corresponds to an absolute change of roughly 22 to 25 events per 100 patients. A large effect size corresponds to a substantial absolute change of approximately 31 to 38 events per 100 patients.

Strong priors based on arbitrary effect size values were designed solely to assess the robustness of our data across a wide range of prior values and were not considered clinically plausible.

For flat/non-informative analysis, we used priors centred at log(OR) = 0 with SD = 1000. For informative priors, the prior mean was derived from expected effect sizes defined using Cohen's h, a standardised measure of difference in proportions. We categorised effect sizes as follows: small (h = 0.2), moderate (h = 0.4), and large (h = 0.8). Expected treatment effects were converted to log(OR) values using the arcsine square root transformation, assuming known event rates in the control (COT) group, 38.6% for the primary outcome and 60.7% for the secondary outcome.

All models were run using four Markov Chain Monte Carlo (MCMC) chains with 20,000 iterations each. Convergence was assessed using the Gelman–Rubin statistic (R-hat) and by visual inspection of trace plots and overlay density plots, generated using the bayesplot package [16, 17].

Meta-analysis-derived informed priors

To derive an informative prior distribution, we performed a frequentist meta-analysis based on escalation data reported by Seow et al., who found that HFNT reduced escalation to IMV (risk ratio (RR) 0.85; 95% confidence interval (CI) 0.76–0.95; p = 0.004) and NIV (RR 0.69, 95% CI 0.49, 0.99; p = 0.04) compared to COT in patients with acute respiratory failure [18].

Data on escalation to both non-invasive and invasive mechanical ventilation were extracted from published forest plots and combined.

Using the meta R package, we performed a quantitative synthesis using a random-effects model with the inverse-variance method and the restricted maximum-likelihood estimator for tau2, based on data from 36 studies, 8428 patients, and 3091 escalation events[5, 19–53]. The random-effects model estimated the effect size as OR 0.8 (95% CI 0.59 −1.07, p-value 0.13). The quantitative synthesis showed signs of heterogeneity, with $I^2 = 73.2\%$ (CI 62.8—80.7%; Supplementary Fig. 1). Based on these results, we developed a model based on an informed normal prior centred at log (OR) = −0.22 with SD = 0.15.

We extracted data from a systematic review by Wang et al. that focused on patients with acute respiratory failure due to COVID-19 undergoing HFNO or conventional oxygen therapy, with escalation to IMV as the primary outcome [54].

We performed a frequentist meta-analysis of observational studies of COVID-19 patients and a separate meta-analysis of RCT data [5, 22, 28–30, 40, 47, 49, 55–62].

The quantitative synthesis of observational studies included 9 studies, 3005 patients, 1782 events (Supplementary Fig. 2).

The random-effects model estimated the effect size as OR 0.52 (95% CI 0.35 −0.78, p-value 0.0013) with significant heterogeneity, $I^2 = 81.1\%$ (CI 65.1—89.8%).

Based on these results, we developed a model based on an informed normal prior centred at log (OR) = −0.63 with SD = 0.20.

The quantitative synthesis of randomised studies included 6 studies, 2180 patients, 835 events (Supplementary Fig. 3).

The random-effects model estimated the effect size as OR 0.8 (95% CI 0.59—1.07, p-value 0.1359) with significant heterogeneity, $I^2 = 47.9\%$ (CI 0—79.3%).

Based on these results, we developed a model based on an informed normal prior centred at log (OR) = −0.23 with SD = 0.15.

We also performed a Bayesian meta-analysis of COVID-19 RCTs using the bayesmeta package [63]. The meta-analysis was based on an informed a priori using the results of the aforementioned pooling of nonrandomised data. The Bayesian meta-analysis estimated the mean posterior effect size as OR 0.65 (95% CrI 0.47—0.88), with significant heterogeneity ($I^2 = 59\%$, Supplementary Fig. 4).

Based on these results, we developed a model based on an informed normal prior centred at log (OR) = −0.43 with SD = 0.16.

To the best of the authors' knowledge, there is insufficient evidence to perform a quantitative synthesis limited to patients with mild COVID-19 respiratory failure, so we considered the aforementioned meta-analyses the best available sources of data for designing our informed priors.

Posterior inference and visualisation

Posterior distributions were summarised using the posterior means and 95% Highest Density Intervals (HDIs) [64]. We visualised the prior, posterior, and approximate likelihood distributions on the log-odds scale. The marginal likelihood was approximated using a profile likelihood method [65]. All plots were generated with ggplot2 package in R [66]. Posterior estimates are reported as OR with corresponding 95% credible intervals (CrI), which represent the range within which the true parameter value lies with 95% probability, given the data and the model.

Region of Practical Equivalence (ROPE)

To guide interpretation of the posterior distributions, we applied the Region of Practical Equivalence (ROPE) framework, following the approach described by Kruschke et al. [64, 67–69]. The ROPE was defined as the range of effect sizes considered clinically negligible, corresponding approximately to a Cohen's h value between + 0.1 and −0.1. For each posterior distribution, we quantified the proportion of the probability mass falling into the following three regions:

- Within the ROPE (no clinically relevant effect),
- Beyond the ROPE in the beneficial direction (potential benefit),
- Beyond the ROPE in the harmful direction, including a predefined threshold for severe harm, set at log(1.25) (corresponding to a 25% increase in odds).

To better quantify the effect size of the ROPE region for the primary outcome, escalation of respiratory support, the effect size corresponds to a reduction or excess of about 5 per 100 treated patients compared with the control. Given limited resources during the COVID-19 pandemic, we believe this effect size is clinically negligible.

Model comparison and Bayes Factor

We compared each pair of models, calculating the Bayes Factor (BF), through the brms package.

The BF represents the ratio of the marginal likelihoods of two models —that is, the probability of the observed data under each model, accounting for their prior distributions. It quantifies the evidence in favour of one hypothesis over another by showing how much more likely the observed data are under one model compared to the other. To categorise the strength of evidence in favour of one model over another, we used Jeffrey's framework for BF interpretation, as reported by Kelter [70, 71].

Quantitative synthesis

We used forest plots to show the posterior estimates and assess consistency across models. The analysis was performed using bayesmeta and ggplot2 packages in R, and we assessed the between-model heterogeneity using the metric tau, which reflects dispersion across model estimates and is influenced by prior specifications [63, 66].

All Bayesian analyses were implemented in R (version 4.5), using the brms package (version 2.22.0), Stan as the backend sampler, and visualisations produced using ggplot2 [11–14, 66]. Custom R code was developed to convert Cohen's h values to log ORs and to generate prior and posterior plots incorporating ROPE assessments. The code used for ROPE visualisations was partially adapted from Zampieri's methodological paper [10].

Results

The analyses conducted revealed varying probabilities of clinical benefit based on different prior models, with substantial evidence supporting modest overall benefits despite significant sensitivity to the chosen prior.

Escalation of respiratory support

Details on the models, priors, and results are reported in Additional file 1 (Supplementary Figs. 4–10 and Supplementary Table 1). The Gelman–Rubin diagnostic (R-hat) values approached unity for all models, indicating satisfactory convergence of the MCMC simulations (see Additional file 1—Supplementary Figs. 12–13). Both bulk Effective Sample Size and tail Effective Sample Size values were sufficiently large relative to the total number of post-warm-up draws, indicating low autocorrelation and reliable estimation of central tendencies and distribution tails.

The flat prior model yielded a posterior estimate corresponding to an OR of approximately 0.69 (Supplementary Fig. 5). The mass probability in the benefit area was 77.5%, and in the ROPE area, 22.1%. Under weak scepticism (SD = 0.8), the probability mass in the clinical benefit range remained relatively high at 74%, with a ROPE probability of 25%. However, as prior scepticism intensified, with intermediate (SD = 0.4) and strong (SD = 0.1) priors, the probability mass on the benefit side declined to 65.8% and 6.3%, respectively, while ROPE probabilities surged to 33.6% and 93.6%, respectively (Supplementary Fig. 5–6).

Under the large-effect optimistic priors, we observed a high proportion of posterior probability allocated to the benefit range (91.6–100%). Optimistic moderate effect and small effect models yielded a high proportion of posterior probability on the clinical benefit side, ranging from 78.9% to 100%.

The Strong Optimistic Small Effect Size Model (mean 0.42, SD 0.1) resulted in a posterior estimate of OR 0.66 (CrI 0.55, 0.79, Supplementary Figs. 7–8).

Under pessimistic models with weak priors, data partially counteracted prior assumptions, with the probability mass in the clinical benefit range ranging from 70% to 53.8%. However, strong pessimistic priors (SD = 0.1) completely overwhelmed the data, yielding a 100% probability of harm (Supplementary Figs. 9–10).

Using the normal prior derived from a combined respiratory failure meta-analysis, including randomised and non-randomised evidence, centred at N(−0.22, 0.15), the posterior mean log odds ratio was −0.27, corresponding to an odds ratio of approximately 0.76 (Fig. 1). The proportion of posterior probability on the benefit side was 70.1%, while 29.9% of the posterior mass laid within the ROPE (Fig. 2). No posterior probability supported harm. This indicates a predominance of clinically relevant

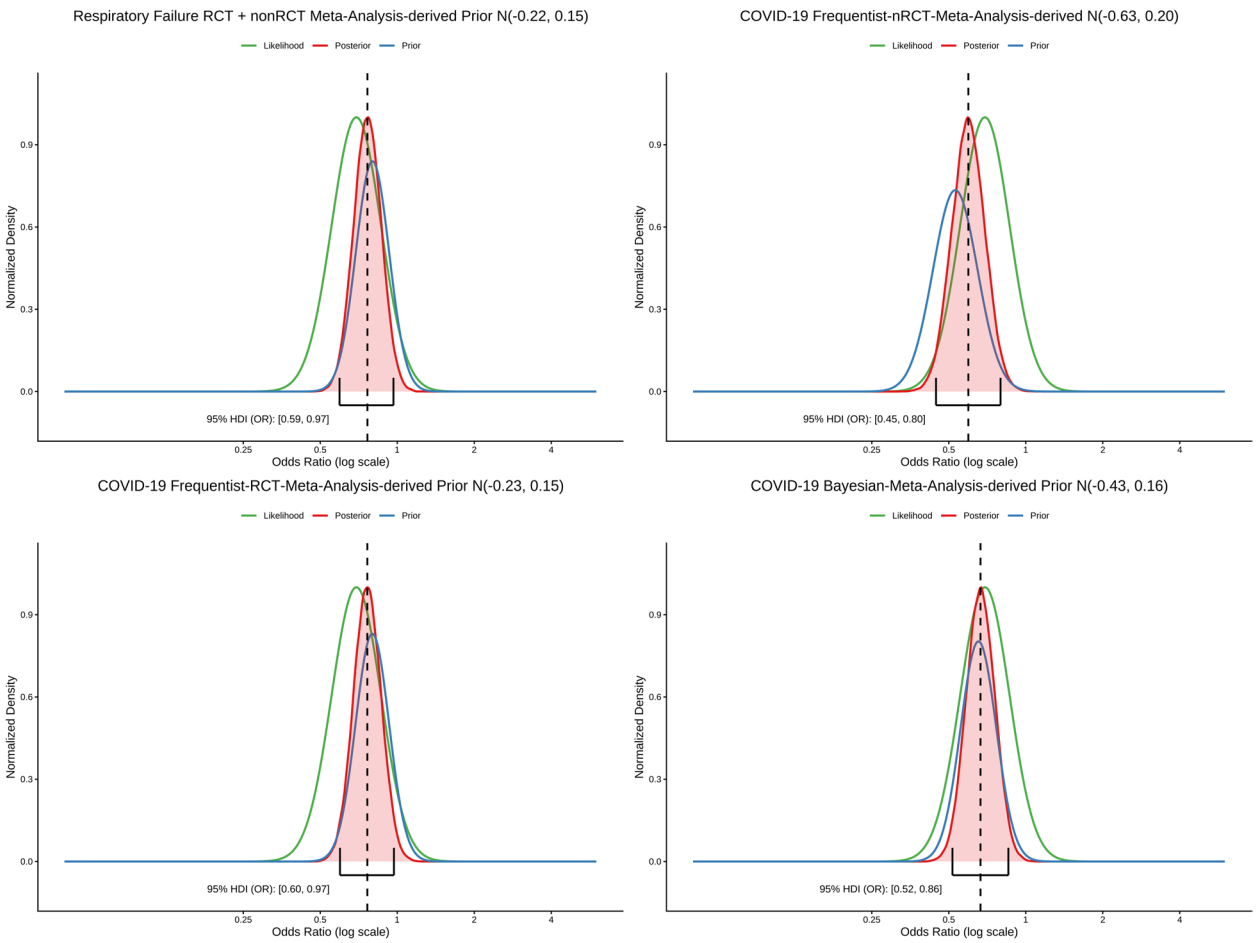

Fig. 1 Panel A. Components of the Meta-analysis-derived models for the primary outcome. This figure illustrates the elements of the Meta-analysis-derived models on the log-odds ratio scale, featuring the prior distribution (blue line), the likelihood function (green line), and the posterior distribution (red). The black horizontal line highlights the 95% highest density interval (HDI) of the posterior estimate

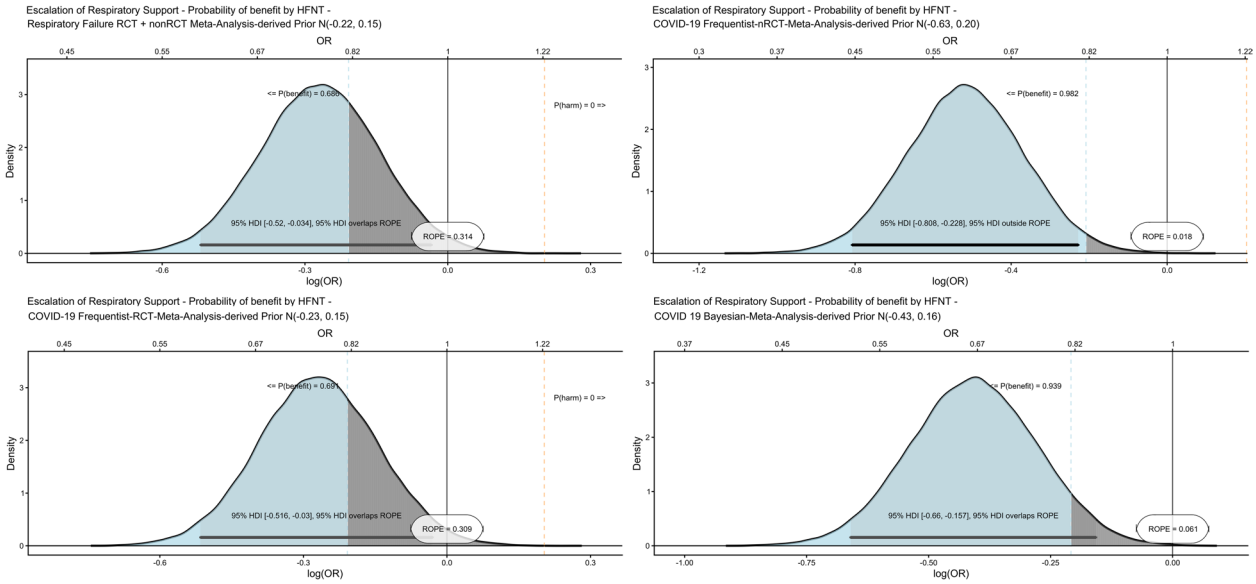

Fig. 2 Analysis of Posterior Distribution derived from Meta-analysis-derived models for the primary outcome for the primary outcome with the Region of Practical Equivalence (ROPE). The figure shows the Posterior distribution of the log odds ratio, highlighting the proportion of the posterior falling into regions of beneficial (light blue), harmful (light orange), and severe harm (dark orange) effects. The black horizontal line highlights the 95% highest density interval (HDI) of the posterior estimate

benefit, though a non-trivial proportion is compatible with no meaningful effect.

The meta-analysis model, derived primarily from non-randomised COVID-19 studies and with a stronger prior centred at N(−0.63, 0.2), yielded a posterior mean of −0.52, corresponding to an odds ratio of approximately 0.60. This model showed very high posterior support for a beneficial effect, with 98.3% of the posterior probability on the beneficial effect side and only 1.7% within the ROPE. No probability mass was located on the harm side.

The meta-analysis models that relied solely on randomised evidence produced more cautious yet consistent results. The frequentist COVID-19 RCT-derived prior N(−0.23, 0.15) returned a posterior mean logOR of −0.27, corresponding to an odds ratio of approximately 0.76. The posterior probability of benefit was 70.5%, with 29.5% within the ROPE and no support for harm. Similarly, the Bayesian COVID-19 meta-analysis derived prior N(−0.43, 0.16) resulted in a posterior mean of −0.41, corresponding to an odds ratio of approximately 0.66, with 94.3% of the posterior probability supporting benefit and 5.7% within the ROPE.

Across all meta-analysis-informed models, posterior probability mass overwhelmingly favoured benefit, with no evidence of harm. Models based on randomised or mixed evidence consistently supported a small to moderate benefit, with residual uncertainty about clinical irrelevance. Still, these three models showed overlap between the HDI and the ROPE, indicating that the null hypothesis cannot be definitively rejected. In contrast, the model informed by non-randomised evidence yielded stronger posterior support for benefit and less probability within the ROPE, also with no overlap between the HDI and the ROPE. Using the strong sceptical null prior (Sk0S N(0, 0.1)) as the reference model to represent the null hypothesis, the Bayes factor results indicate consistent, though generally modest, support for at least a small benefit. The strongest evidence against the null is observed for the Strong Optimistic Small Effect Size model N(−0.42, 0.1), which yields a Bayes factor of 3.07 relative to Sk0S, corresponding to moderate evidence in favour of a small beneficial effect. The Intermediate Optimistic Small Effect Size model N(−0.42, 0.4) also favours benefit, with BF = 1.67 relative to the null, whereas the weak small effect model N(−0.42, 0.8) does not improve fit relative to no difference, with BF = 0.92.

Meta-analysis-informed models showed a coherent and broadly similar pattern. The Bayesian meta-analysis model N(−0.43, 0.16) received moderate support vs the null model with a BF = 2.74 (Supplementary Fig. 11). Meta-analysis models derived from COVID-19 randomised studies and the mixed evidence on acute respiratory failures, centred on N(−0.22, 0.15), perform similarly, with Bayes factors of 2.47 relative to Sk0S. The meta-analysis model, based primarily on non-randomised studies, centred on a larger effect N(−0.63, 0.2), received weaker support, with BF = 1.73 versus the null. Overall, when evaluated against a tight null prior, our

data consistently favoured models with priors centred on modest effect sizes with relatively limited dispersion (Supplementary Figure S15 in the Additional file 1).

Models assuming large or moderate effect sizes, or using flat priors, yielded less consistent support for benefit, as reflected by lower Bayes Factors.

Across models, we found that the pooled posterior effect estimate was centred at log(OR) = −0.25, corresponding to an OR of approximately OR 0.78 (CrI 0.62—0.98), suggesting a modest overall benefit (Fig. 3). However, the level of heterogeneity was notable, with median $\tau = 0.61$ and an associated I^2 of 95%, indicating that the Bayesian estimates were quite sensitive to prior specification.

Clinical recovery

Details on the models, priors, and results are reported in Supplementary Figs. 14–19 and Supplementary Table 2 in the Additional file 1. The Gelman–Rubin diagnostic (R-hat) values were all equal to 1, suggesting satisfactory convergence of the MCMC chains (Supplementary Figs. 21–22 in the Additional file 1). The sceptical models with flat-to-moderate strength priors showed a posterior probability mass on the clinical benefit side ranging from 72.6% to 60.8%. The optimistic models yielded a proportion of the posterior probability lying beyond the ROPE on the beneficial side, ranging from 74.4% to 98.6%. The Strong Optimistic Small Effect Size N (0.42, 0.1) produced a posterior estimate of OR 1.5 (CrI 1.27, 1.83; Fig. 3), with 98.6% of the posterior probability allocated to the clinical benefit range. Pessimistic models showed that evidence of clinical benefit remained robust under weak and intermediate strength targeting small effects, with 65% to 41.9% of the posterior probability within the benefit range, and less than 3% indicating harm. The Strong Optimistic Small Effect Size N (0.42, 0.1) and Intermediate Optimistic Small Effect Size: N (0.42, 0.4) showed robust evidence (BF > 10) against most alternatives (Supplementary Fig. 20 in the Additional file 1). The weakest supporting evidence was observed for both optimistic and pessimistic models assuming large effect sizes, as well as flat prior model.

Quantitative synthesis across models yielded a pooled posterior mean effect of OR 1.23 (CrI 0.94 −1.60) with significant prior-related heterogeneity (Fig. 4).

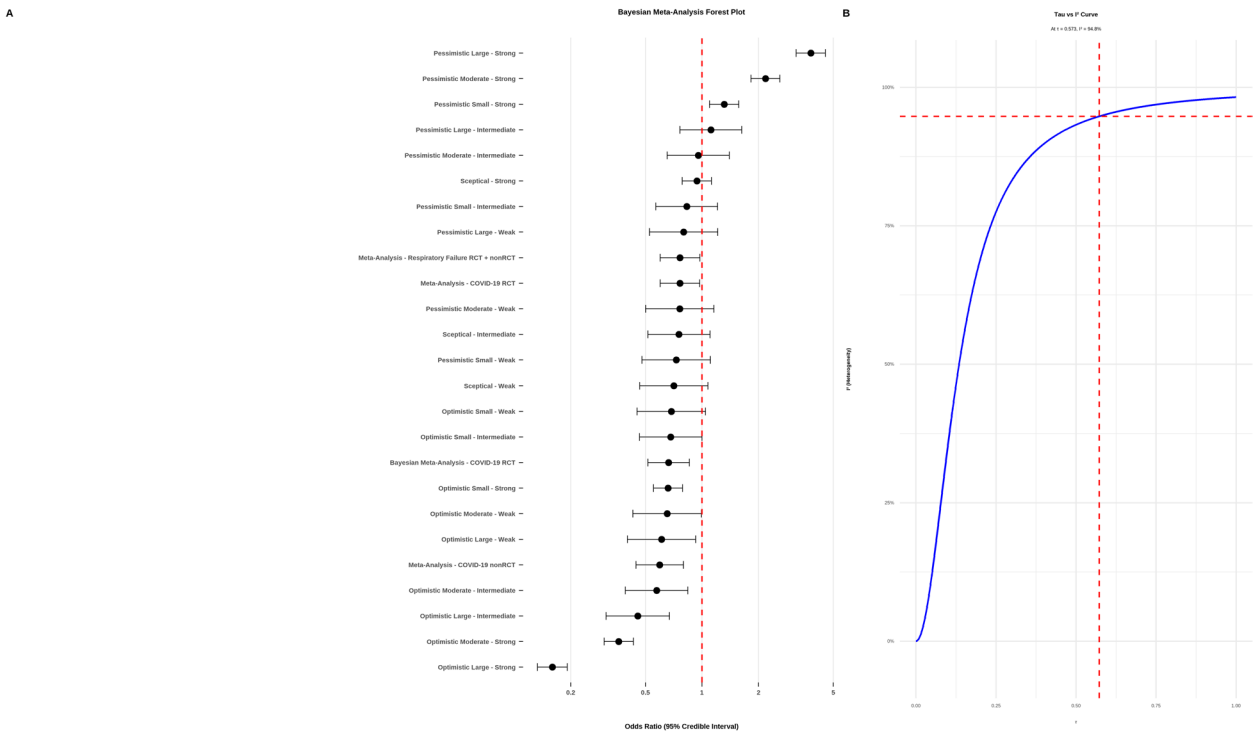

Fig. 3 Panel A. Forest plot showing odds ratios (95% credible intervals) for the escalation of the respiratory support outcome under each different prior specification.. Each point represents the posterior median effect size with horizontal lines indicating 95% credible intervals. The vertical dashed red line at OR = 1 indicates no effect. Effect sizes are presented on a log scale.. Panel B. Tau vs I2 curve illustrating the relationship between the between-study heterogeneity parameter (τ) and the I2 statistic. The vertical red dashed line indicates the posterior median τ value, while the horizontal red dashed line shows the corresponding I2 value

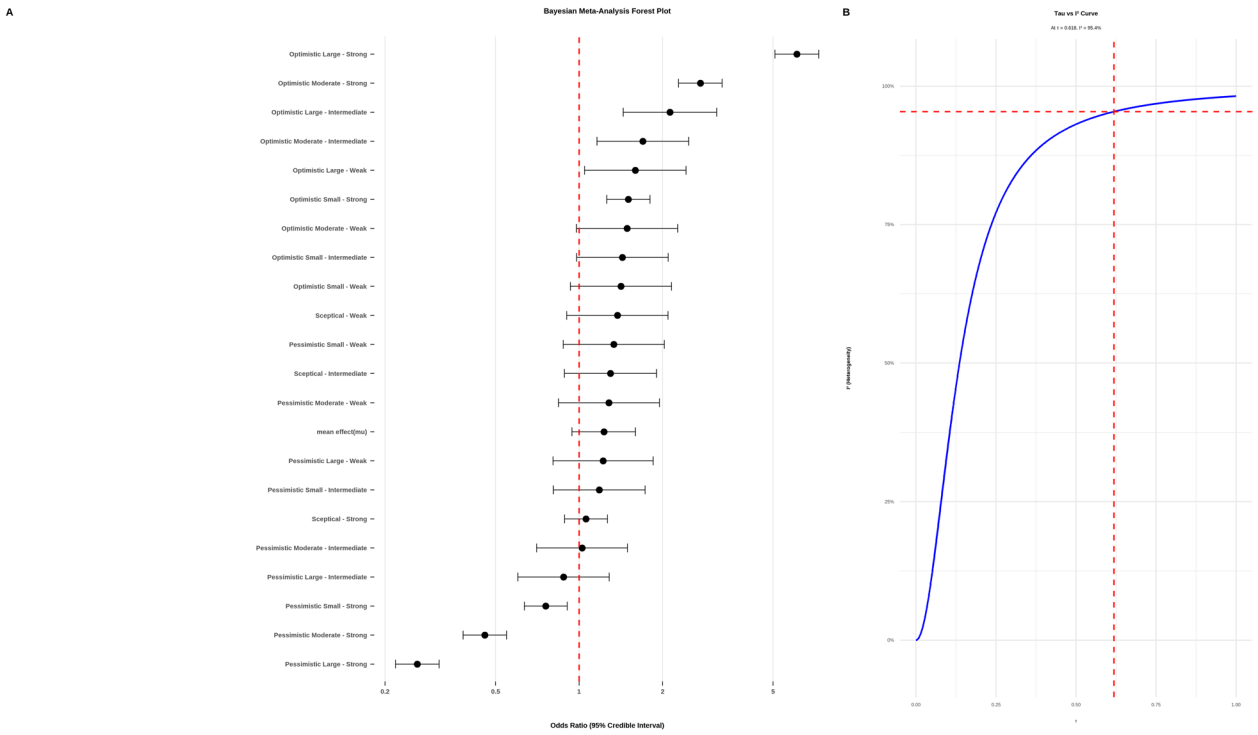

Fig. 4 Panel A. Forest plot showing odds ratios (95% credible intervals) for the clinical improvement outcome under each different prior specification.. Each point represents the posterior median effect size with horizontal lines indicating 95% credible intervals. The vertical dashed red line at OR = 1 indicates no effect. Effect sizes are presented on a log scale.. Panel B. Tau vs I2 curve illustrating the relationship between the between-study heterogeneity parameter (τ) and the I2 statistic. The vertical red dashed line indicates the posterior median τ value, while the horizontal red dashed line shows the corresponding I2 value

Discussion

In this post hoc analysis of the COVID-HIGH trial, we used a Bayesian approach to re-interpret the original results. Our analysis suggests a high probability that HFNT is clinically beneficial compared to COT in reducing the need for escalation of respiratory support.

Across a wide range of prior assumptions – from flat to optimistic – the posterior probability mass on the clinical benefit side remained high (generally > 70%), while the posterior probability mass on the clinically meaningful harm side remained consistently low (≤ 6%) across all models, underscoring a favourable benefit-risk profile. Even under weakly sceptical priors, the data suggested a substantial likelihood of clinical benefit. Although strong sceptical priors could attenuate the observed effect, these scenarios represent assumptions that are not aligned with the available empirical evidence. Moreover, under weak to intermediate sceptical models, HFNT promotes timely clinical recovery, with a probability mass in the benefit region ranging from 61 to 73%. These findings mitigate the conclusion of the original frequentist analysis, which may overlook potentially meaningful effects [8]. Therefore, we sought to better characterise the likelihood of clinical benefit or harm associated with the use of HFNT in patients with COVID-19 pneumonia and mild hypoxaemia in a probabilistic framework.

Unlike p-values, which provide binary outcomes, our Bayesian approach quantifies the probability mass lying on the side of benefit or harm, offering clinicians a more intuitive basis for decision-making [72].

These Bayesian findings should be interpreted as complementary to the primary frequentist analysis of the COCID-HIGH trial.

Across multiple meta-analysis-informed prior specifications, results were consistent and favoured a reduction in escalation of respiratory support. Using a respiratory failure meta-analysis combining randomised and non-randomised studies, the posterior log odds ratio was − 0.27, corresponding to an odds ratio of approximately 0.76, with 70.1% of the posterior probability supporting benefit and 29.9% within the ROPE.

Similar results were observed when restricting the prior to randomised COVID-19 evidence. The COVID-19 RCT frequentist meta-analysis prior yielded a posterior

odds ratio of approximately 0.76, with 70.5% of probability mass in the benefit area and 29.5% within the ROPE. The Bayesian COVID-19 RCT meta-analysis, incorporating information from non-randomised studies, produced a stronger effect on the posterior effect size, with an odds ratio of approximately 0.66 and 94.3% posterior probability supporting benefit, with only 5.7% within the ROPE.

The meta-analysis-derived prior, based predominantly on non-randomised COVID-19 studies, showed the largest effect, with a posterior odds ratio of approximately 0.60 and a 98.3% posterior probability supporting benefit. Across all meta-analysis designs, no posterior probability supported harm, indicating robust support for benefit with varying degrees of certainty depending on the source of prior information. Among all the meta-analysis models, only the COVID-19 non-randomised informed prior showed HDI values outside the ROPE region.

These findings support existing international guidelines suggesting the efficacy of HFNT in reducing intubation or escalation of care in acute respiratory failure and are particularly relevant when considered in the context of the COVID-19 pandemic, during which ICU resources were often critically limited [2, 3, 73].

The findings of the present study align with a growing body of literature supporting the use of Bayesian approaches in critical care trials, particularly in situations where modest or lower-than-expected event rates compromise statistical power. The increasing adoption of Bayesian methods in critical care trials reflects a shift toward more informative, decision-oriented interpretations of clinical evidence [74]. Several high-profile RCTs in intensive care, such as ANDROMEDA-SHOCK, EOLIA, and RECOVERY, have been reanalysed using a Bayesian approach to address the limitations of conventional frequentist null hypothesis testing, especially in the context of modest effect sizes [75–77]. These re-analyses have shown that trials deemed "negative" by conventional standards may still suggest high probabilities of clinically meaningful benefit when viewed through a Bayesian framework. Our findings contribute to this evolving methodological landscape, reinforcing the value of probabilistic inference in trials with lower-than-expected event rates or underpowered designs, which are common challenges in acute care research.

The application of the ROPE allowed us to further assess the degree to which treatment effects were clinically meaningful. In most models, only a minority of posterior probability fell within the ROPE, suggesting that the observed effects of HFNT are unlikely to be clinically negligible. Still, many models showed an HDI interval that partially overlapped the ROPE, so we cannot definitely reject the null hypothesis. These findings were quite robust across most models, and models incorporating optimistic small effect priors and meta-analytic data were supported by strong evidence, as shown by Bayes factors > 10 in most pairwise comparisons with other models, suggesting substantial evidence supporting the benefit of HFNT over COT.

These results should be interpreted in the context of recent observational studies of HFNT in COVID-19–related AHRF which report variable escalation rates, respiratory support strategies, and clinical outcomes across different care pathways [78, 79]. These studies highlight the heterogeneity of clinical trajectories and management strategies in COVID-19-related AHRF, which should be considered when interpreting the COVID-HIGH findings. In this context, a Bayesian approach helps integrate uncertainty and clinical variability when interpreting treatment effects in practice.

Furthermore, real-world data show an association between positive-pressure non-invasive ventilation and adverse events, such as barotrauma, within the conceptual framework of Patient-Self-Inflicted Lung Injury (P-SILI). Compared with COT, HFNT is not associated with an increased risk of this complication, making it a particularly attractive technique for use in lower-intensity care settings [78].

Strengths and limitations of this study

The strengths of this reanalysis lie in its comprehensive modelling strategy, inclusion of external evidence, and formal application of Bayesian decision tools such as ROPE and Bayes factors. Moreover, the general strengths of the COVID-HIGH trial, including international recruitment and complete follow-up data, also apply to this analysis. However, this study has several limitations. This was a post hoc re-analysis of the COVID-HIGH trial and was not pre-specified in the original trial protocol. Although all priors were selected based on clinical rationale and external data from existing literature, specifying priors in Bayesian modelling involves a degree of subjectivity, as conclusions depend on both the observed data and the chosen prior distributions. To mitigate this, we explored a wide range of priors, including flat, sceptical, and optimistic priors, as well as one informed by a recent meta-analysis, to assess the consistency and robustness of our findings across varying prior assumptions. Finally, although COVID-HIGH focused on patients with mild hypoxaemia (PaO_2/FiO_2 200–300 mmHg), where treatment effects may be smaller and more heterogeneous, the consistency of benefit across our Bayesian models suggests that HFNT may be particularly valuable in settings where the use of noninvasive respiratory support could delay or prevent escalation. The absolute difference in escalation was 6.6%, indicating that for every 15 patients treated with HFNT instead of COT, one patient would

avoid escalation. Overall, these findings have important implications for clinicians. They enhance the interpretability of clinical trial data, offering alternative perspectives that closely reflect the natural process of weighing risks and benefits at the bedside, resembling intuitive clinical reasoning, especially in resource-constrained environments or amid future respiratory pandemics [75].

Finally, this Bayesian reanalysis focused on prespecified clinical outcomes of the original COVID-HIGH trial and should be interpreted within the specific context of patients with COVID-19–related mild AHRF. Future studies should prospectively evaluate the applicability of these findings in other clinical settings and the potential role of dynamic physiological indices, such as the ratio of pulse oximetry/fraction of inspired oxygen to respiratory rate, ROX index, in identifying patients most likely to benefit from HFNT in mild AHRF across different clinical contexts [80].

Conclusions

This Bayesian re-analysis of the COVID-HIGH trial suggests that HFNT likely reduces the need for escalation of respiratory support and promotes timely clinical recovery in patients with COVID-19-pneumonia and mild hypoxaemia, with minimal probability of harm. Uncertainty remains, as the magnitude of this effect was sensitive to prior assumptions and frequently included values compatible with clinically negligible benefit.

Abbreviations

AHRF	Acute Hypoxaemic Respiratory Failure
BF	Bayes Factor
CI	Confidence Interval
COT	Conventional Oxygen Therapy
CPAP	Continuous Positive Airway Pressure
CrI	Credible Interval
FiO_2	Fraction of Inspired Oxygen
HDI	95% Highest Density Interval
HFNT	High-Flow Nasal Therapy
ICU	Intensive Care Unit
IMV	Invasive Mechanical Ventilation
I^2	Between-Model Heterogeneity Measure (I-squared)
MCMC	Markov Chain Monte Carlo
NIV	Noninvasive Ventilation
OR	Odds Ratio
PaO_2	Partial Pressure of Arterial Oxygen
PaO_2/FiO_2	Ratio of Arterial Oxygen Partial Pressure to Fraction of Inspired Oxygen
RCT	Randomised Controlled Trial
R-hat	Gelman–Rubin Convergence Diagnostic Statistic
ROPE	Region of Practical Equivalence
RR	Risk Ratio
SD	Standard Deviation
SpO_2	Peripheral Capillary Oxygen Saturation

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s44158-026-00361-3.

Supplementary Material 1.

Acknowledgements

Collaborators of the COVID-HIGH trial are the following COVID-HIGH Investigators:

Drs. Stefano De Vuono, Sokol Berisha, Patrizia Pierini, Maria Rita Taliani, Francesco Balducci, Pasquale Cianci, Alessandra Lignani from Emergency Department, Santa Maria della Misericordia Hospital, Perugia, Italy; Drs. Pasquale Imitazione, Angela Mirizzi, Anna Annunziata, Antonietta Coppola, Francesca Simioli, Antonella Marotta from UOC Fisiopatologia e Riabilitazione Respiratoria AO dei Colli, Naples, Italy; Drs. Konstantinos Gourgoulianis, Athanasios Pagonis, Konstantinos Tourlakopoulos from Department of Respiratory Medicine, Faculty of Medicine, University of Thessaly, Larissa, Greece; Drs. Eleni Laou from Department of Anesthesiology, Faculty of Medicine, University of Thessaly, Larisa, Greece; Drs. Alessandro Libra, Ada Vancheri, Nicola Ciancio, Pietro Impellizzeri, Rossella Intravaia from Respiratory Medicine Unit, Policlinico "G. Rodolico-San Marco" University Hospital, Catania, Italy; Drs. Ernesto Crisafulli, Giulia Sartori from Respiratory Medicine Unit, Department of Medicine, University of Verona, Verona, Italy; Drs. Valentina Musella, Leonello Fuso, Luciana Paladini, Gabriele Valli from UOC Malattie Apparato Respiratorio ed Endoscopia Bronchiale, AO San Giovanni, Roma, Italy; Drs. José Pedro Boléo-Tomé, Énia Ornelas, Miguel Filipe Guia from Pulmonology Department, Hospital Prof. Doutor Fernando Fonseca, Amadora, Portugal; Drs. Chiara Chiappero, Marco Bardessono, Mauro Mangiapia from Cardio-Thoracic Department, AOU Città della Salute e della Scienza, Molinette Hospital, Turin, Italy; Drs. Margherita Marelli, Cinzia Gambarini, Dania Mazzola, Giuditta Riganti from UO Pneumologia ASST-Settelaghi, Varese, Italy; Drs. Alberto Perboni, Sara Demichelis, Massimo Comune, Giulia Rovere from Pulmonology Department; San Luigi Gonzaga Hospital, Orbassano (TO), Italy; Drs. Luca Guidelli, Giacomo Ghinassi, Nicoletta Golfi from Pulmonology and Respiratory Intensive Care Unit, S. Donato Hospital, Arezzo, Italy; Drs. Antonella Spacone, Antonietta Esposito, Giorgia Rapacchiale from Respiratory Medicine Unit, General Hospital, Pescara, Italy; Drs. Antonio Voza, Carlo Fedeli, Sara Sauro from Dipartimento di Medicina d'Urgenza, Istituto Clinico Humanitas Research Hospital, Milano, Italy; Drs. Gianfilippo Gangitano, Ilaria Gessaroli, Davide Francia from AUSL Romagna, Emergency Department, Infermi Hospital, Rimini; Drs. Pablo Flórez, Cristina Lalmolda from Pneumology Service, Hospital de Sabadell, Spain, CIBERES; Drs. Valentina Pinelli, Stefania Artioli, Massimiliano Meazza from Division of Pneumology, Ospedale San Bartolomeo, Sarzana, La Spezia, Italy; Drs. Donato Lacedonia, Giulia Scioscia, Marcello Stomaci from Department of Medical and Surgical Sciences, "Policlinico Riuniti" University Hospital, University of Foggia, Italy; Drs. Silvia Marani, Mara Bozzoli from Medicina Interna, Ospedale Ramazzini, Carpi, Ausl Modena, Italy; Dr. Mehmet Nuri Yakar from Dokuz Eylul University, Department of Pulmonary and Critical Care, İzmir, Turkey; Drs. Elisiana Carpagnano, Valentina Di Lecce from Institute of Respiratory Disease, Department of Basic Medical Science, Neuroscience, and Sense Organs, University of Bari "Aldo Moro", Bari, Italy; Drs. Erika Zanardi, Monica Trentin from Aulss 7 Pedemontana, Ospedale Santorso, Santorso (VI), Italia; Drs. Szymon Skoczyński, Aleksandra Oraczewska from Department of Pneumonology, Faculty of Medical Sciences in Katowice, Medical University of Silesia—Katowice, Poland; Drs. Marco Contoli, Brunilda Marku from Respiratory Section, Department of Translational Medicine, University of Ferrara, Italy; Drs. Paola Noto, Eugenia Di Fazio from Emergency Medicine Unit, AOU Policlinico "G. Rodolico-San Marco" University Hospital, Catania, Italy; Drs. Pierachille Santus, Dejan Radovanovic from Division of Respiratory Diseases, Ospedale Luigi Sacco, ASST Fatebenefratelli-Sacco, Department of Biomedical and Clinical Sciences (DIBIC), University of Milan, Italy; Dr. Luigi Marino, U.O. Pneumotisiologia, Ospedale di Vittorio Veneto, ULSS 2 Marca Trevigiana, Vittorio Veneto, Treviso, Italy.

Authors' contributions

Claudia Crimi: Conceptualisation, Methodology, Validation, Data curation, Writing – Original Draft, Writing – Review & Editing. Salvatore Sardo: Conceptualisation, Methodology, Software, Validation, Formal analysis, Data curation, Writing – Original Draft, Writing – Review & Editing. Alberto Noto: Methodology, Validation, Data curation, Writing – Review & Editing. Fabiana Madotto: Conceptualisation, Methodology, Validation, Data curation, Writing – Original Draft, Writing – Review & Editing. Mariachiara Ippolito: Validation, Data curation, Writing – Original Draft, Writing – Review & Editing. Santi Nolasco: Data curation, Writing – Original Draft, Writing – Review & Editing. Raffaele Campisi: Data curation, Writing – Review & Editing. Giuseppe Fiorentino: Data curation, Writing – Review & Editing. Ioannis Pantazopoulos: Data curation, Writing – Review & Editing. Athanasios Chalkias: Conceptualisation, Methodology,

Writing – Review & Editing. Alessio Mattei: Data curation, Writing – Review & Editing. Raffaele Scala: Data curation, Writing – Review & Editing. Enrico Clini: Data curation, Writing – Review & Editing. Begum Ergan: Data curation, Writing – Review & Editing. Manel Lujan: Data curation, Writing – Review & Editing. João Carlos Winck: Data curation, Writing – Review & Editing. Antonino Giarratano: Data curation, Writing – Review & Editing. Annalisa Carlucci: Data curation, Writing – Review & Editing. Cesare Gregoretti: Data curation, Writing – Review & Editing. Paolo Groff: Conceptualisation, Writing – Review & Editing. Andrea Cortegiani: Conceptualisation, Methodology, Validation, Data curation, Writing – Original Draft, Writing – Review & Editing, Supervision. All authors contributed to the data analysis and interpretation, critical revision of the publication, and final approval to submit. AC, CC, AN, FM, and SS have accessed and verified the data in this study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Funding
There was no funding source for this study.

Data availability
Deidentified participant data are available upon reasonable request. We provided an excerpt of the code for constructing Bayesian linear models in the Supplementary Analysis.

Declarations

Ethics approval and consent to participate
The study protocol of the original COVID-HIGH trial was approved by the Ethics Committee of the coordinating centre (Comitato Etico Catania 1, 01/2021/PO, 25/01/2021) and all participating sites before patient inclusion. The study was performed in accordance with Good Clinical Practice guidelines and ethical principles of the Declaration of Helsinki. The trial was overseen by an oversight committee comprised of independent clinicians with no competing interests. Written informed consent was obtained from all patients or surrogates.

Consent for publication
The patients provided informed consent for inclusion in the COVID-HIGH trial and for the analysis and dissemination of results.

Competing interests
A Ca received consulting fees from Breas, Airliquide, honoraria for lectures or consultancies from Fisher & Paykel, Philips, ResMed, Vitalaire (outside the submitted work). CC participated in an advisory board from Airliquide and received honoraria for lectures from Fisher & Paykel, Philips, ResMed, Vitalaire, and Medicair (outside the submitted work). CG received honoraria for lectures or consultancies from Vivisol and Air Liquide (outside the submitted work). BE received financial support for attending meetings from Fisher & Paykel. EC received grants from Chiesi Italia, honoraria for lectures from Chiesi Italia, GSK, Boehringer Ingelheim, and financial support for attending meetings from Chiesi Italia, Boehringer Ingelheim. IP received honoraria for lectures and financial support for attending meetings from Fisher & Paykel, Chiesi, Elpen, AstraZeneca, Menarini, and Pfizer (outside the submitted work). JCW received a consulting fee from Inogen, honoraria for lectures from Fisher & Paykel, Philips, payment for testimony from Philips, and financial support for attending meetings from Vitalaire (outside the submitted work). A Co and FM are Associate Editors for Journal of Anesthesia Analgesia and Critical Care.

Author details
[1]Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy. [2]Respiratory Intensive Care Unit, Respiratory Medicine Unit, Policlinico "G. Rodolico-San Marco" University Hospital, Catania, Italy. [3]Department of Medical Sciences and Public Health, University of Cagliari, Monserrato, Italy. [4]Department of Human Pathology of the Adult and Evolutive Age "Gaetano Barresi", Division of Anesthesia and Intensive Care, University of Messina, Policlinico "G. Martino", Messina, Italy. [5]Department of Anesthesia, Critical Care and Emergency, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy. [6]Department of Precision Medicine in Medical, Surgical and Critical Care Area (Me.Pre.C.C.), University of Palermo, Palermo, Italy. [7]Department of Anesthesia, Intensive Care and Emergency, Policlinico Paolo Giaccone University Hospital, Palermo, Italy. [8]UOC Fisiopatologia E Riabilitazione Respiratoria AO Dei Colli, Naples, Italy. [9]Department of Emergency Medicine, Faculty of Medicine, University of Thessaly, Larisa, Greece. [10]Institute for Translational Medicine and Therapeutics, University of Pennsylvania Perelman School of Medicine, Philadelphia, USA. [11]OUTCOMES RESEARCH Consortium®, Houston, TX, USA. [12]Department of Critical Care Medicine, Tzaneio General Hospital, Piraeus, Greece. [13]Department of "Medical Area", Respiratory Medicine Unit, Santa Croce E Carle Hospital, Cuneo, AO, Italy. [14]Pulmonology and Respiratory Intensive Care Unit, S. Donato Hospital, Arezzo, Italy. [15]Respiratory Diseases Unit, Department of Medical and Surgical Sciences SMECHIMAI, University Hospital of Modena Policlinico, University of Modena Reggio Emilia, Modena, Italy. [16]Department of Pulmonary and Critical Care, Dokuz Eylul University, İzmir, Turkey. [17]Department of Respiratory Medicine, Parc Taulí Hospital Universitari, Institut d'Investigació i Innovació Parc Taulí (I3PT-CERCA), Universitat Autònoma de Barcelona, Sabadell, Spain. [18]Cardiovascular R&D Centre (UniC), Faculdade de Medicina da Universidade Do Porto, Porto, Portugal. [19]Pulmonology Unit, Instituto CUF Porto, Porto, Portugal. [20]Department of Experimental Medicine, University of Salento, Lecce, Italy. [21]Pulmonary Unit, Vito Fazzi Hospital, Lecce, Italy. [22]Intensive Care Unit, Fondazione 'Giglio', Cefalù, Palermo, Italy. [23]Unicamillus International University, Rome, Italy. [24]Emergency Department, "S. Maria Della Misericordia" Hospital, Perugia, Italy.

Received: 10 November 2025 Accepted: 9 February 2026
Published online: 21 February 2026

References

1. RENOVATE Investigators and the BRICNet Authors, Francio F, Weigert RM, Mattei EDB, Grion CMC, Festti J, et al. High-flow nasal oxygen vs noninvasive ventilation in patients with acute respiratory failure: the RENOVATE randomized clinical trial. JAMA. 2025;333(10):875.
2. Rochwerg B, Einav S, Chaudhuri D, Mancebo J, Mauri T, Helviz Y et al (2020) The role for high flow nasal cannula as a respiratory support strategy in adults: a clinical practice guideline. Intensive Care Med 46(12):2226–2237
3. Oczkowski S, Ergan B, Bos L, Chatwin M, Ferrer M, Gregoretti C et al (2022) ERS clinical practice guidelines: high-flow nasal cannula in acute respiratory failure. Eur Respir J 59(4):2101574
4. Grieco DL, Menga LS, Cesarano M, Rosà T, Spadaro S, Bitondo MM et al (2021) Effect of helmet noninvasive ventilation vs high-flow nasal oxygen on days free of respiratory support in patients with COVID-19 and moderate to severe hypoxemic respiratory failure: the HENIVOT randomized clinical trial. JAMA 325(17):1731
5. Perkins GD, Ji C, Connolly BA, Couper K, Lall R, Baillie JK et al (2022) Effect of noninvasive respiratory strategies on intubation or mortality among patients with acute hypoxemic respiratory failure and COVID-19: the RECOVERY-RS randomized clinical trial. JAMA 327(6):546
6. Ospina-Tascón GA, Martínez D, Gempeler A (2022) High-flow oxygen vs conventional oxygen and invasive mechanical ventilation and clinical recovery in patients with severe COVID-19—reply. JAMA 327(11):1092
7. Crimi C, Pierucci P, Renda T, Pisani L, Carlucci A (2022) High-flow nasal cannula and COVID-19: a clinical review. Respir Care 67(2):227–240
8. Crimi C, Noto A, Madotto F, Ippolito M, Nolasco S, Campisi R et al (2023) High-flow nasal oxygen versus conventional oxygen therapy in patients with COVID-19 pneumonia and mild hypoxaemia: a randomised controlled trial. Thorax 78(4):354–361
9. Patel M, Gangemi A, Marron R, Chowdhury J, Yousef I, Zheng M et al (2020) Retrospective analysis of high flow nasal therapy in COVID-19-related moderate-to-severe hypoxaemic respiratory failure. BMJ Open Respir Res 7(1):e000650
10. Zampieri FG, Casey JD, Shankar-Hari M, Harrell FE, Harhay MO (2021) Using bayesian methods to augment the interpretation of critical care trials. An overview of theory and example reanalysis of the alveolar recruitment for acute respiratory distress syndrome trial. Am J Respir Crit Care Med. 203(5):543–52
11. R Core Team R. R: A language and environment for statistical computing. 2013;
12. Bürkner PC (2017) brms : an *R* package for Bayesian multilevel models using *Stan*. J Stat Softw 80(1):1–28
13. Bürkner PC (2018) Advanced Bayesian multilevel modeling with the R package brms. R J 10(1):395

14. Bürkner PC (2021) Bayesian item response modeling in *R* with brms and *Stan*. J Stat Softw 100(5):1–54
15. Carpenter B, Gelman A, Hoffman MD, Lee D, Goodrich B, Betancourt M et al (2017) Stan: a probabilistic programming language. J Stat Softw 76:1–32
16. Gabry J, Simpson D, Vehtari A, Betancourt M, Gelman A (2019) Visualization in Bayesian Workflow. J R Stat Soc Ser A Stat Soc 182(2):389–402
17. Gelman A, Rubin DB (1992) Inference from Iterative Simulation Using Multiple Sequences. Stat Sci 7(4):457–472
18. Seow D, Khor YH, Khung SW, Smallwood DM, Ng Y, Pascoe A et al (2024) High-flow nasal oxygen therapy compared with conventional oxygen therapy in hospitalised patients with respiratory illness: a systematic review and meta-analysis. BMJ Open Respir Res 11(1):e002342
19. Andino R, Vega G, Pacheco SK, Arevalillo N, Leal A, Fernández L, et al. High-flow nasal oxygen reduces endotracheal intubation: a randomized clinical trial. Ther Adv Respir Dis. 2020;14(NA):1753466620956459.
20. N ApltekiNoğlu MendiL, Ş Temel, RC Yüksel, K Gündoğan, B Eser, L Kaynar et al (2021) The use of high-flow nasal oxygen vs. standard oxygen therapy in hematological malignancy patients with acute respiratory failure in hematology wards. Turk J Med Sci 51(4):1756–63
21. Azoulay E, Lemiale V, Mokart D, Nseir S, Argaud L, Pène F et al (2018) Effect of high-flow nasal oxygen vs standard oxygen on 28-day mortality in immunocompromised patients with acute respiratory failure: the HIGH randomized clinical trial. JAMA 320(20):2099
22. Bonnet N, Martin O, Boubaya M, Levy V, Ebstein N, Karoubi P et al (2021) High flow nasal oxygen therapy to avoid invasive mechanical ventilation in SARS-CoV-2 pneumonia: a retrospective study. Ann Intensive Care 11(1):37
23. Branick K, Jackson JA, McCann D, Pelaez CA, Pruett WM, Spilman SK, et al. Use of nasal high flow oxygen on the general medical floor can prevent ICU admission and escalation of care in COPD patients. In: B24 Critical care: gone with the wind - Mechanical ventilation: hfnc, niv and invasive . American Thoracic Society; 2019. p. A2733–A2733. Available from: https://doi.org/10.1164/ajrccm-conference.2019.199.1_MeetingAbstracts.A2733. Cited 2025 Dec 25.
24. COVID-ICU Group on behalf of the REVA Network and the COVID-ICU Investigators. Clinical characteristics and day-90 outcomes of 4244 critically ill adults with COVID-19: a prospective cohort study. Intensive Care Med. 2021;47(1):60–73.
25. Demoule A, Vieillard Baron A, Darmon M, Beurton A, Géri G, Voiriot G et al (2020) High-flow nasal cannula in critically Ill patients with severe COVID-19. Am J Respir Crit Care Med 202(7):1039–1042
26. for the Efraim investigators and the Nine-I study group, Azoulay E, Pickkers P, Soares M, Perner A, Rello J, et al. Acute hypoxemic respiratory failure in immunocompromised patients: the efraim multinational prospective cohort study. Intensive Care Med. 2017;43(12):1808–19.
27. Frat JP, Coudroy R, Marjanovic N, Thille AW (2017) High-flow nasal oxygen therapy and noninvasive ventilation in the management of acute hypoxemic respiratory failure. Ann Transl Med 5(14):297–297
28. Frat JP, Quenot JP, Badie J, Coudroy R, Guitton C, Ehrmann S et al (2022) Effect of high-flow nasal cannula oxygen vs standard oxygen therapy on mortality in patients with respiratory failure due to COVID-19: the SOHO-COVID randomized clinical trial. JAMA 328(12):1212
29. Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S et al (2015) High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. N Engl J Med 372(23):2185–2196
30. Gallardo A, Dévoli AP, Arévalo GEB, Saavedra SN, Moracci RS, Pratto RA et al (2022) High-flow nasal cannula and standard oxygen in acute hypoxemic respiratory failure due to COVID-19. Respir Care 67(12):1534–1541
31. Gedikloglu M, Gulen M, Satar S, Icen YK, Avci A, Yesiloglu O et al (2022) How to treat patients with acute respiratory failure? Conventional oxygen therapy versus high-flow nasal cannula in the emergency department. Hong Kong J Emerg Med 29(2):84–93
32. Geng W, Batu W, You S, Tong Z, He H (2020) High-flow nasal cannula: a promising oxygen therapy for patients with severe bronchial asthma complicated with respiratory failure. Can Respir J 2020(1):1–7
33. Jones PG, Kamona S, Doran O, Sawtell F, Wilsher M (2016) Randomized controlled trial of humidified high-flow nasal oxygen for acute respiratory distress in the emergency department: the HOT-ER study. Respir Care 61(3):291–299
34. Lee M, Kim JH, Jeong IB, Son JW, Na MJ, Kwon SJ (2019) Protecting postextubation respiratory failure and reintubation by high-flow nasal cannula compared to low-flow oxygen system: single center retrospective study and literature review. Acute Crit Care 34(1):60–70
35. Lemiale V, De Jong A, Dumas G, Demoule A, Mokart D, Pène F et al (2020) Oxygenation strategy during acute respiratory failure in critically-ill immunocompromised patients. Crit Care Med. 48(9):e768-75
36. Lemiale V, Mokart D, Mayaux J, Lambert J, Rabbat A, Demoule A et al (2015) The effects of a 2-h trial of high-flow oxygen by nasal cannula versus venturi mask in immunocompromised patients with hypoxemic acute respiratory failure: a multicenter randomized trial. Crit Care 19(1):380–388
37. Lemiale V, Resche-Rigon M, Mokart D, Pène F, Argaud L, Mayaux J et al (2017) High-flow nasal cannula oxygenation in immunocompromised patients with acute hypoxemic respiratory failure: a groupe de recherche respiratoire en réanimation onco-hématologique study. Crit Care Med 45(3):e274–e280
38. Macé J, Marjanovic N, Faranpour F, Mimoz O, Frerebeau M, Violeau M et al (2019) Early high-flow nasal cannula oxygen therapy in adults with acute hypoxemic respiratory failure in the ED: a before-after study. Am J Emerg Med 37(11):2091–2096
39. Maggiore SM, Idone FA, Vaschetto R, Festa R, Cataldo A, Antonicelli F et al (2014) Nasal high-flow versus venturi mask oxygen therapy after extubation. Effects on oxygenation, comfort, and clinical outcome. Am J Respir Crit Care Med. 190(3):282–8
40. Mohd Kamil MK, Yuen Yoong KP, Noor Azhar AM, Bustam A, Abdullah AH, Md Yusuf MH, et al. Non-rebreather mask and low-flow nasal cannula vs high-flow nasal cannula in severe COVID-19 pneumonia in the emergency department. Am J Emerg Med. 2023;63(NA):86–93.
41. Pugh R, Ingley S, Ellison A. EPM. 119 nasal high flow oxygen for community-acquired pneumonia. J Intensive Care Soc. 2016;
42. Rittayamai N, Tscheikuna J, Praphruetkit N, Kijpinyochai S (2015) Use of high-flow nasal cannula for acute dyspnea and hypoxemia in the emergency department. Respir Care 60(10):1377–1382
43. Roca O, De Acilu MG, Caralt B, Sacanell J, Masclans JR (2015) Humidified high flow nasal cannula supportive therapy improves outcomes in lung transplant recipients readmitted to the intensive care unit because of acute respiratory failure. Transplantation 99(5):1092–1098
44. Ruangsomboon O, Limsuwat C, Praphruetkit N, Monsomboon A, Chakorn T, Hiestand BC E (2021) Nasal high-flow oxygen versus conventional oxygen therapy for acute severe asthma patients: a pilot randomized controlled trial. Acad Emerg Med 28(5):530–541
45. S South Yorkshire Hospitals Research Collaboration, Bateman RM, Sharpe MD, Jagger JE, Ellis CG, Solé-Violán J, et al. 36th international symposium on intensive care and emergency medicine: brussels, belgium. 15–18 march 2016. Crit Care. 2016 Apr;20(S2):94, s13054–016–1208–6.
46. Saeed A, Wagih K, Huusein N. Evaluation of nasal optiflow device in management of COPD patients in acute exacerbations. In: European Respiratory Journal [Internet]. European Respiratory Society; 2015. p. PA2170. Available from: https://doi.org/10.1183/13993003.congress-2015.PA2170. Cited 2025 Dec 25.
47. Sayan İ, Altınay M, Çınar AS, Türk HŞ, Peker N, Şahin K et al (2021) Impact of HFNC application on mortality and intensive care length of stay in acute respiratory failure secondary to COVID-19 pneumonia. Heart Lung 50(3):425–429
48. Song HZ, Gu JX, Xiu HQ, Cui W, Zhang GS (2017) The value of high-flow nasal cannula oxygen therapy after extubation in patients with acute respiratory failure. Clinics 72(9):562–567
49. Thota B, Samantaray A, B V, Mangu HR, Alladi M, Kalawat U. A randomised controlled trial of high-flow nasal oxygen versus non-rebreathing oxygen face mask therapy in acute hypoxaemic respiratory failure. Indian J Anaesth. 2022;66(9):644–50.
50. Ting-Yu Hu, Chao-Hsien Lee, Kuang-Hua Cheng, Mei-Chu Tan, Hsiao-Fang Hua, Li-Kuo Kuo. Effect of high-flow nasal oxygen vs. Conventional oxygen therapy on extubation outcomes and physiologic changes for patients with high risk of extubation failure in the medical ICU: a tertiary center, randomized, controlled trial. Int J Gerontol. 2020;14(1):36.
51. Xia J, Gu S, Lei W, Zhang J, Wei H, Liu C et al (2022) High-flow nasal cannula versus conventional oxygen therapy in acute COPD exacerbation with mild hypercapnia: a multicenter randomized controlled trial. Crit Care 26(1):109–119

52. Xia M, Li W, Yao J, Jin Y, Du G, Xu Q et al (2021) A postoperative comparison of high-flow nasal cannula therapy and conventional oxygen therapy for esophageal cancer patients. Ann Palliat Med 10(3):2530–2539
53. Xing D, Chen YH, Wang LT, Yu B, Ran ZB, Chen L (2021) Evaluation of the therapeutic effect of high-flow nasal cannula oxygen therapy on patients with aspiration pneumonia accompanied by respiratory failure in the post-stroke sequelae stage. BMC Pulm Med 21(1):17–25
54. Wang J chao, Peng Y, Dai B, Hou H jia, Zhao H wen, Wang W, et al. Comparison between high-flow nasal cannula and conventional oxygen therapy in COVID-19 patients: a systematic review and meta-analysis. Ther Adv Respir Dis. 2024:17534666231225323.
55. Bouadma L, Mekontso-Dessap A, Burdet C, Merdji H, Poissy J, Dupuis C, et al. High-dose dexamethasone and oxygen support strategies in intensive care unit patients with severe COVID-19 acute hypoxemic respiratory failure: the COVIDICUS randomized clinical trial. JAMA Intern Med. 2022;182(9):906.
56. COVID-ICU group, for the REVA network, COVID-ICU investigators, Schmidt M, Demoule A, Hajage D, Pham T, Combes A, et al. Benefits and risks of noninvasive oxygenation strategy in COVID-19: a multicenter, prospective cohort study (COVID-ICU) in 137 hospitals. Crit Care. 2021;25(1):421.
57. Department of Anesthesiology and Critical Care, Government Institute of Medical Sciences, Greater Noida, Uttar Pradesh, India, Nazir A, Saxena A, Department of Anesthesiology and Critical Care, Government Institute of Medical Sciences, Greater Noida, Uttar Pradesh, India. The effectiveness of high-flow nasal cannula and standard non-rebreathing mask for oxygen therapy in moderate category COVID-19 pneumonia: randomised controlled trial. Afr J Thorac Crit Care Med. 2022;28(1):9–14.
58. Gough C, Casey M, McCartan TA, Franciosi AN, Nash D, Doyle D, et al. Effects of non-invasive respiratory support on gas exchange and outcomes in COVID-19 outside the ICU. Respir Med. 2021;185(NA):106481.
59. Ospina-Tascón GA, Calderón-Tapia LE, García AF, Zarama V, Gómez-Álvarez F, Álvarez-Saa T et al (2021) Effect of high-flow oxygen therapy vs conventional oxygen therapy on invasive mechanical ventilation and clinical recovery in patients with severe COVID-19: a randomized clinical trial. JAMA 326(21):2161
60. Teng X bao, Shen Y, Han M feng, Yang G, Zha L, Shi J feng. The value of high-flow nasal cannula oxygen therapy in treating novel coronavirus pneumonia. Eur J Clin Invest. 2021;51(3):e13435.
61. Wendel Garcia PD, Aguirre-Bermeo H, Buehler PK, Alfaro-Farias M, Yuen B, David S et al (2021) Implications of early respiratory support strategies on disease progression in critical COVID-19: a matched subanalysis of the prospective RISC-19-ICU cohort. Crit Care Lond Engl 25(1):175
62. Wendel-Garcia PD, Mas A, González-Isern C, Ferrer R, Máñez R, Masclans JR et al (2022) Non-invasive oxygenation support in acutely hypoxemic COVID-19 patients admitted to the ICU: a multicenter observational retrospective study. Crit Care 26(1):37
63. Röver C (2020) Bayesian random-effects meta-analysis using the bayesmeta *R* package. J Stat Softw 93(6):1–51
64. Kruschke JK (2018) Rejecting or Accepting Parameter Values in Bayesian Estimation. Adv Methods Pract Psychol Sci 1(2):270–280
65. Reid N (1996) Likelihood and Bayesian Approximation Methods. In: Bernardo JM, Berger JO, Dawid AP, Smith AFM (eds) Bayesian Statistics 5. Oxford University PressOxford, pp 351–368
66. Wickham H, Sievert C (2009) Ggplot2: elegant graphics for data analysis, vol 10. Springer New York
67. Kruschke JK (2011) Bayesian Assessment of Null Values Via Parameter Estimation and Model Comparison. Perspect Psychol Sci 6(3):299–312
68. Kruschke JK (2013) Bayesian estimation supersedes the t test. J Exp Psychol Gen 142(2):573–603
69. Kruschke JK, Liddell TM (2018) The Bayesian New Statistics: Hypothesis testing, estimation, meta-analysis, and power analysis from a Bayesian perspective. Psychon Bull Rev 25(1):178–206
70. Jeffreys H (1998) The theory of probability. OuP Oxford
71. Kelter R (2020) Bayesian alternatives to null hypothesis significance testing in biomedical research: a non-technical introduction to Bayesian inference with JASP. BMC Med Res Methodol 20(1):142
72. Ruberg SJ (2021) Détente: a practical understanding of P values and bayesian posterior probabilities. Clin Pharmacol Ther 109(6):1489–1498
73. Grasselli G, Calfee CS, Camporota L, Poole D, Amato MBP, Antonelli M et al (2023) ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies. Intensive Care Med 49(7):727
74. Yarnell CJ, Abrams D, Baldwin MR, Brodie D, Fan E, Ferguson ND et al (2021) Clinical trials in critical care: can a bayesian approach enhance clinical and scientific decision making? Lancet Respir Med 9(2):207–216
75. Goligher EC, Tomlinson G, Hajage D, Wijeysundera DN, Fan E, Jüni P et al (2018) Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome and posterior probability of mortality benefit in a post hoc bayesian analysis of a randomized clinical trial. JAMA 320(21):2251
76. Zampieri FG, Damiani LP, Bakker J, Ospina-Tascón GA, Castro R, Cavalcanti AB, et al. Effects of a resuscitation strategy targeting peripheral perfusion status versus serum lactate levels among patients with septic shock. A bayesian reanalysis of the ANDROMEDA-SHOCK trial. Am J Respir Crit Care Med. 2020;201(4):423–9.
77. Lee TC, McDonald EG, Butler-Laporte G, Harrison LB, Cheng MP, Brophy JM (2021) Remdesivir and systemic corticosteroids for the treatment of COVID-19: a bayesian re-analysis. Int J Infect Dis 104:671–676
78. Vetrugno L, Castaldo N, Fantin A, Deana C, Cortegiani A, Longhini F et al (2023) Ventilatory associated barotrauma in COVID-19 patients: a multicenter observational case control study (COVI-MIX-study). Pulmonology 29(6):457–468
79. Ranieri VM, Tonetti T, Navalesi P, Nava S, Antonelli M, Pesenti A et al (2022) High-Flow Nasal Oxygen for Severe Hypoxemia: Oxygenation Response and Outcome in Patients with COVID-19. Am J Respir Crit Care Med 205(4):431–439
80. Roca O, Messika J, Caralt B, García-de-Acilu M, Sztrymf B, Ricard JD et al (2016) Predicting success of high-flow nasal cannula in pneumonia patients with hypoxemic respiratory failure: The utility of the ROX index. J Crit Care 1(35):200–205

Publisher's Note