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Original article

Noninvasive ventilation versus oxygen mask for preoxygenation before emergency tracheal intubation in critically ill adults: Systematic review and meta-analysis

Ventilación no invasiva versus mascarilla de oxígeno para la preoxigenación antes de la intubación traqueal de emergencia en adultos críticamente enfermos: revisión sistemática y metaanálisis

Alvaro Andre Vargas Aguilar[a,b], Jose Luis Villca Villegas[a,*], Sinaí Fernanda Claros Rocabado[a,b], Gustavo Irusta[c]

[a] *Faculty of Health Sciences, Universidad Franz Tamayo, Cochabamba, Bolivia*
[b] *School of Medicine, Universidad Franz Tamayo, Cochabamba, Bolivia*
[c] *Hospital de Clínicas José de San Martín, University of Buenos Aires, Argentina*

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ABSTRACT

Objective: To compare the effectiveness and safety of noninvasive ventilation (NIV) versus standard oxygen mask for preoxygenation before emergency intubation in critically ill adults.
Design: Systematic review and meta-analysis of randomized clinical trials following PRISMA 2020. Protocol registered in PROSPERO (CRD420251028685). Risk ratios (RR) were calculated using random-effects models with HKSJ adjustment. Certainty assessed using GRADE.
Setting: Intensive care units and emergency departments. Only in-hospital settings were included.
Patients or participants: 1619 critically ill adults requiring emergency intubation from four RCTs (802 NIV, 817 standard mask). Mean age ranged from 55 to 65 years across trials; 79% enrolled in ICUs, 21% in EDs.
Interventions: Preoxygenation with NIV (CPAP or bilevel positive airway pressure) versus standard passive face-mask oxygenation without positive pressure.
Main variables of interest: Primary outcome: peri-intubation hypoxemia (SpO2 < 80%). Safety outcome: aspiration or regurgitation.
Results: Peri-intubation hypoxemia occurred in 63/802 (7.9%) with NIV versus 144/817 (17.6%) with mask (RR 0.39; 95% CI 0.14–1.04; $p = 0.08$; $I^2 = 55\%$). The point estimate favored NIV, but the confidence interval crossed unity under the HKSJ-adjusted model. Three of four trials individually showed significant reductions. Aspiration was infrequent (1.0% vs 1.7%; $p = 0.31$). Certainty was moderate for hypoxemia and low for safety.
Conclusions: Preoxygenation with NIV did not significantly reduce peri-intubation hypoxemia compared with a standard oxygen mask under the HKSJ-adjusted model. Nonetheless, the pooled point estimate favored NIV and three of the four trials showed significant reductions, suggesting a possible benefit that did not reach statistical significance. No increases in adverse events were observed. The decision to use NIV should be individualized according to clinical context, patient profile, and team experience.

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Abbreviations: CI, Confidence interval; CPAP, Continuous positive airway pressure; ED, Emergency department; FiO2, Fraction of inspired oxygen; GLMM, Generalized linear mixed model; GRADE, Grading of Recommendations Assessment, Development and Evaluation; HFNO, High-flow nasal oxygen; ICU, Intensive care unit; NIV, Noninvasive ventilation; PEEP, Positive end-expiratory pressure; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT, Randomized controlled trial; REML, Restricted maximum likelihood; RoB 2, Cochrane Risk of Bias 2 tool; RR, Risk ratio; SpO2, Peripheral oxygen saturation.

* Corresponding author.
E-mail addresses: consultor.alvaro.vargas@unifranz.edu.bo (A.A.V. Aguilar), jvillcavillegas@gmail.com (J.L.V. Villegas).

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Palabras clave:
Ventilación no invasiva
Intubación traqueal
Hipoxemia
Preoxigenación
Enfermedad crítica

RESUMEN

Objetivo: Comparar la eficacia y seguridad de la ventilación no invasiva (VNI) frente a la mascarilla estándar para la preoxigenación antes de la intubación de emergencia en adultos críticamente enfermos.
Diseño: Revisión sistemática y metaanálisis de ensayos clínicos aleatorizados según PRISMA 2020. Protocolo registrado en PROSPERO (CRD420251028685). Se calcularon RR mediante efectos aleatorios con ajuste HKSJ. Certeza evaluada con GRADE.
Ámbito: Unidades de cuidados intensivos y urgencias. Solo se incluyeron entornos intrahospitalarios.
Pacientes o participantes: 1.619 adultos críticamente enfermos de cuatro ensayos aleatorizados (802 VNI, 817 mascarilla). Edad media 55–65 años; 79% en UCI, 21% en urgencias.
Intervenciones: Preoxigenación con VNI (CPAP o presión positiva binivel) versus mascarilla facial estándar sin presión positiva.
Variables de interés principales: Desenlace primario: hipoxemia periintubación (SpO2 < 80%). Desenlace de seguridad: aspiración o regurgitación.
Resultados: Hipoxemia periintubación: 63/802 (7,9%) con VNI frente a 144/817 (17,6%) con mascarilla (RR 0,39; IC 95%: 0,14–1,04; p = 0,08; I^2 = 55%). El estimador puntual favoreció a la VNI, pero el intervalo de confianza cruzó la unidad bajo el modelo HKSJ. Tres de cuatro ensayos mostraron reducciones significativas. Aspiración infrecuente (1,0% vs 1,7%; p = 0,31). Certeza moderada para hipoxemia y baja para seguridad.
Conclusiones: La VNI no redujo de forma estadísticamente significativa la hipoxemia periintubación frente a la mascarilla estándar bajo el modelo ajustado por HKSJ. No obstante, el estimador puntual favoreció a la VNI y tres de los cuatro ensayos mostraron reducciones significativas, lo que sugiere un posible beneficio que no alcanzó significación estadística. No se observaron aumentos de eventos adversos. La decisión debe individualizarse según el contexto clínico, el perfil del paciente y la experiencia del equipo.

Introduction

Emergency tracheal intubation in critically ill adults carries a high risk of immediate adverse events. Peri-intubation hypoxemia and hemodynamic instability are common and are associated with major complications, including cardiac arrest and death, particularly in intensive care units (ICUs) and emergency departments (EDs).[1–3] Clinical syntheses and observational cohorts have confirmed the impact of these events, including the association between hypotension/hypoxemia and peri-intubation arrest.[4,5] Moreover, national audits, multicenter series, and international studies have reported high rates of severe hypoxemia, cardiovascular instability, and cardiac arrest during out-of-operating-room intubations.[6–12]

Preoxygenation is a key safety component before anesthetic induction; its aim is to maximize oxygen reserves and prolong the ”safe” apnea time. In patients with respiratory failure, techniques that combine high inspired oxygen fractions with positive pressure—such as continuous positive airway pressure (CPAP) or noninvasive ventilation (NIV)—and high-flow oxygen devices can increase functional residual capacity and enhance alveolar recruitment, thereby mitigating peri-procedural desaturation.[13,14] Contemporary guidelines recommend standardizing preparation, equipment, and device selection, with explicit emphasis on preventing desaturation throughout the entire peri-intubation period.[15]

Despite the widespread adoption of preoxygenation, clinical uncertainty remains regarding the comparative effectiveness of strategies that use positive pressure (NIV) versus standard facemask preoxygenation without positive pressure in this high-risk setting. Therefore, this systematic review and meta-analysis aims to compare the effectiveness and safety of NIV with standard facemask preoxygenation in critically ill adults undergoing emergency intubation in the ICU or ED, with a focus on its effect on the incidence of hypoxemia. The research question was structured according to the PICO framework: Population (P), critically ill adults requiring emergency tracheal intubation in the ICU or ED; Intervention (I), preoxygenation with NIV (including CPAP and bilevel positive airway pressure modes); Comparator (C), standard passive facemask oxygenation without positive pressure (i.e., a non-rebreather mask or simple facemask connected to an oxygen source, excluding manual bag-valve-mask ventilation with positive pressure); and Outcome (O), incidence of peri-intubation hypoxemia.

Methods

We conducted a systematic review and meta-analysis and reported it in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.[32,34] The PRISMA 2020 checklist is provided as Supplementary material (Supplementary Table S1). The protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO; CRD420251028685). The protocol was registered on April 9, 2025, before the initiation of study screening.

Eligibility criteria

Studies were considered eligible for inclusion when meeting all of the following criteria: (I) randomized controlled trials (RCTs); (II) comparing NIV versus standard facemask preoxygenation; (III) in critically ill adults in the ICU/ED setting; and (IV) reporting hypoxemia as an outcome (preferred definition: SpO2 < 85%). Different NIV interfaces/modalities and usual preoxygenation intervals (3–5 min) were accepted. Standard facemask preoxygenation was defined as passive oxygenation with a facemask (non-rebreather or simple mask with reservoir) connected to a high-flow oxygen source, without the application of positive pressure; manual ventilation with a bag-valve-mask device delivering positive pressure was not considered a “standard facemask” method in the comparator arm. Only in-hospital settings (ICU and ED) were eligible; studies conducted entirely in prehospital environments were excluded. Exclusion criteria were: non-randomized studies or studies without a standard facemask control group, elective intubations, pediatric populations, exclusively prehospital settings, lack of a defined hypoxemia outcome, or studies with overlapping populations where a more comprehensive report was available. None of the included studies enrolled patients whose intubation was initiated outside the hospital; all procedures were performed within the ICU or ED.

Search strategy and data extraction

We searched PubMed/MEDLINE, Cochrane CENTRAL, Web of Science, and Scopus databases from inception to 21 October 2025, with no date or language restrictions. We also searched ClinicalTrials.gov and screened the reference lists of eligible studies and prior systematic re-

views. The full search strategies for each database are reported in the Supplementary material (Supplementary Table S2).

Records were managed in Zotero (automatic deduplication plus manual verification) and then imported into a systematic review platform (Covidence) for two-stage screening by two independent reviewers (titles and abstracts, then full text). Disagreements were resolved by consensus or by a third reviewer. Reasons for full-text exclusion were documented, and a PRISMA flow diagram was prepared. Data extraction was performed in duplicate using a standardized, pilot-tested form capturing study characteristics, population demographics, intervention/comparator details, outcome definitions and data, and methodological features.

Outcomes

The main efficacy outcome was peri-intubation hypoxemia, defined as SpO2 < 80%. All four included trials reported this threshold, allowing a single pooled analysis.

Safety outcomes included aspiration pneumonia or regurgitation during the procedure.

Risk of bias assessment

Two reviewers (JLVV and AAVA) independently assessed the risk of bias for each RCT using the Cochrane Risk of Bias 2 (RoB 2) tool,[23] covering: randomization sequence generation/allocation concealment, deviations from intended interventions, missing outcome data, outcome measurement (objective for SpO2), and selective reporting. Any disagreements were resolved by consensus or by a third reviewer (SFCR). Where appropriate, we also considered analyses restricted to studies at low risk of bias.

Certainty assessment

Certainty of the evidence was assessed per outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.[35–38] The outcomes were categorized as very low, low, moderate, or high certainty based on the presence of risk of bias, inconsistency of results, imprecision, publication bias, and magnitude of treatment effects.

Statistical analyses

For dichotomous outcomes, we estimated risk ratios (RRs) with 95% confidence intervals (CIs) using a random-effects model with inverse-variance weighting, τ^2 estimated by restricted maximum likelihood (REML), and study-level variance based on log (RR). In case zero-event cells were observed, we applied rare-event models (Peto or generalized linear mixed model [GLMM]) or continuity corrections.[29] Statistical heterogeneity was quantified using I^2 and τ^2. If heterogeneity was present ($I^2 > 25\%$), we explored sources of variability through univariable meta-regression with year of publication as the moderator and presented the result with a bubble plot.

Small-study effects were assessed using Egger's regression test and a weighted funnel plot.[27,28] Given the small number of pooled trials, the Hartung–Knapp–Sidik–Jonkman (HKSJ) adjustment was applied to the random-effects model as the primary basis for statistical inference, as it yields more reliable coverage than the conventional Wald method when few studies are combined.[31] As sensitivity analyses, we performed leave-one-out procedures and compared the HKSJ-adjusted estimates with conventional REML-based confidence intervals.[33] All analyses were conducted in R (version 4.3.2) using the "metafor"[30] and "meta" packages.

Results

We identified 337 records through databases and registries. After removing duplicates, 165 records remained for screening. Following title/abstract and full-text review, four studies met the inclusion criteria and were incorporated into the review and meta-analysis, comprising 1661 randomized patients (Fig. 1); of these, 1619 (802 in the NIV group and 817 in the mask group) contributed to the primary pooled analysis of peri-intubation hypoxemia, the 42-patient difference reflecting missing outcome data in Baillard 2018 ($n = 2$) and PREOXI ($n = 40$). Detailed reasons for exclusion at the full-text stage are provided in Supplementary Table S3. The five studies excluded after full-text assessment were removed for the following reasons: wrong intervention ($n = 1$), study protocol without outcome data ($n = 2$), wrong comparator ($n = 1$), and duplicate protocol of an excluded trial ($n = 1$); detailed descriptions are available in Supplementary Table S3. Regarding the clinical setting, the majority of patients were enrolled in ICUs ($n = 1312$; 79.0%), whereas 349 patients (21.0%) were enrolled in EDs, the latter exclusively from the PREOXI trial, which was the only multicenter study including both settings. Mean age ranged from 55 to 65 years across studies. Different NIV modalities were used, including CPAP and bilevel positive airway pressure (BiPAP). Baseline characteristics are presented in Table 1.

Efficacy outcomes

For peri-intubation severe hypoxemia ($SpO_2 < 80\%$), four RCTs were pooled comprising 802 patients in the NIV group and 817 in the standard oxygen mask group. The incidence was 63/802 (7.9%) in the NIV group versus 144/817 (17.6%) in the mask group (RR 0.39; 95% CI 0.14–1.04; $p = 0.08$; $I^2 = 55\%$; $\tau^2 = 0.2373$; Fig. 3). Although the point estimate favored NIV, the confidence interval crossed unity, indicating that the pooled difference did not reach statistical significance at the 0.05 level under the random-effects model with the Hartung–Knapp–Sidik–Jonkman adjustment. Individually, three of the four trials (Baillard 2006, Nong 2020, and Gibbs 2024) showed statistically significant reductions in hypoxemia favoring NIV, whereas Baillard 2018 did not reach significance.

Safety outcomes

Aspiration events were reported in three trials. Pooled analysis showed aspiration occurred in 8/771 patients (1.0%) in the NIV group versus 13/784 patients (1.7%) in the mask group (RR 0.64; 95% CI 0.27–1.51; $p = 0.31$; $I^2 = 0\%$). The low event rates resulted in wide confidence intervals that preclude definitive conclusions regarding aspiration risk.

Risk of bias assessment

Two RCTs were judged as low risk and two were judged as having some concerns in the overall risk of bias based on the RoB 2 assessment tool. The main reasons for concerns were issues with missing outcome data and selective outcome reporting. The results for the risk of bias are detailed in Fig. 2.

Certainty of evidence

According to the GRADE assessment, severe hypoxemia (SpO2 < 80%) was classified as moderate-certainty evidence, downgraded one level for imprecision, as the pooled 95% confidence interval was compatible with both a meaningful reduction and no effect. Safety outcomes (aspiration or regurgitation) were classified as low-certainty evidence, downgraded for very serious imprecision arising from the low event rates (Table 2).

Table 1
Characteristics of included studies.

Author (Year)	Design/Setting	Population	N (NIV:Mask)	Intervention (NIV)	Comparator (Mask)	Preox. Duration	Main Outcome	Key Hypoxemia Result	Registration/Funding
Baillard et al. (2006)[19]	RCT, 2 medical-surgical ICUs (France)	Adults with acute hypoxemic respiratory failure requiring intubation; mean age ~62 years; ~32% female	53 (27:26)	NIV with PSV, PEEP 5 cmH2O, FiO2 100% via ICU ventilator and face mask	Non-rebreather mask with reservoir, O2 15 L/min	3 min	Severe hypoxemia SpO2 <80% during intubation	2/27 (7%) NIV vs 12/26 (46%) mask	No registration; no funding declared; no COI
Baillard et al. (2018)[17]	Multicenter RCT, ICU (France)	Adults with acute hypoxemic respiratory failure requiring intubation; median age 65 (57–74) NIV vs 62 (53–74) mask; ~33% female	201(98:101)[a]	NIV (PSV adjusted to 6–8 mL/kg), PEEP 5 cmH2O, FiO2 100%	Mask with reservoir, O2 15 L/min	3 min	Severe hypoxemia SpO2 <80% during intubation (secondary endpoint)	18/98 (18.4%) NIV vs 28/101 (27.7%) mask (p≈0.10)	NCT00472160; funded by AP-HP/French Ministry of Health (PHRC)
Nong et al. (2020)	RCT, ICU (China)	Hypoxemic adults requiring intubation; mean age 55–57 ± 14 years; ~29% female	106 (53:53)	NIV via oronasal mask connected to ventilator with fiberoptic bronchoscopy port (nasotracheal intubation)	Mask with reservoir (standard control)	3 min	Hypoxemia SpO2 <80% during intubation	4/53 (7.5%) NIV vs 20/53 (37.7%) mask	No registration reported; funding not specified
Gibbs et al. (2024)[16] (PREOXI)	Pragmatic multicenter RCT, ICU and ED (USA)	Critically ill adults requiring intubation; median age 61 years; 39-40% female	1301 (624:637)	NIV (ICU or dedicated NIV ventilator; CPAP/PS with PEEP; operator-selected parameters)	Oxygen mask (bag-reservoir or simple; per local practice)	Not standardized (per local practice)	Severe hypoxemia SpO2 < 85% from induction to 2 min post-intubation	39/624 (6.2%) NIV vs 84/637 (13.2%) mask	NCT05267652; funded by U.S. Department of Defense

Abbreviations: RCT, randomized controlled trial; ICU, intensive care unit; ED, emergency department; NIV, noninvasive ventilation; PSV, pressure support ventilation; PEEP, positive end-expiratory pressure; FiO2, fraction of inspired oxygen; SpO2, peripheral oxygen saturation; CPAP, continuous positive airway pressure; PS, pressure support; COI, conflict of interest; AP-HP, Assistance Publique–Hôpitaux de Paris; PHRC, Programme Hospitalier de Recherche Clinique.

[a] 201 patients were randomized (99 NIV, 102 mask); two patients were excluded from the hypoxemia analysis due to missing SpO2 data, yielding 98 and 101 patients analyzed in the NIV and mask groups, respectively. Similarly, for Gibbs 2024, 1301 patients were randomized (645 NIV, 656 mask), but the primary outcome was available for 624 and 637 patients, respectively. The primary outcome of Gibbs 2024 (PREOXI) was severe hypoxemia SpO2 < 85% (57/624 [9.1%] NIV vs 118/637 [18.5%] mask; Δ −9.4 pp; $p < 0.001$); the "Key Hypoxemia Result" column reports the exploratory SpO2 <80% data for consistency with the pooled analysis.

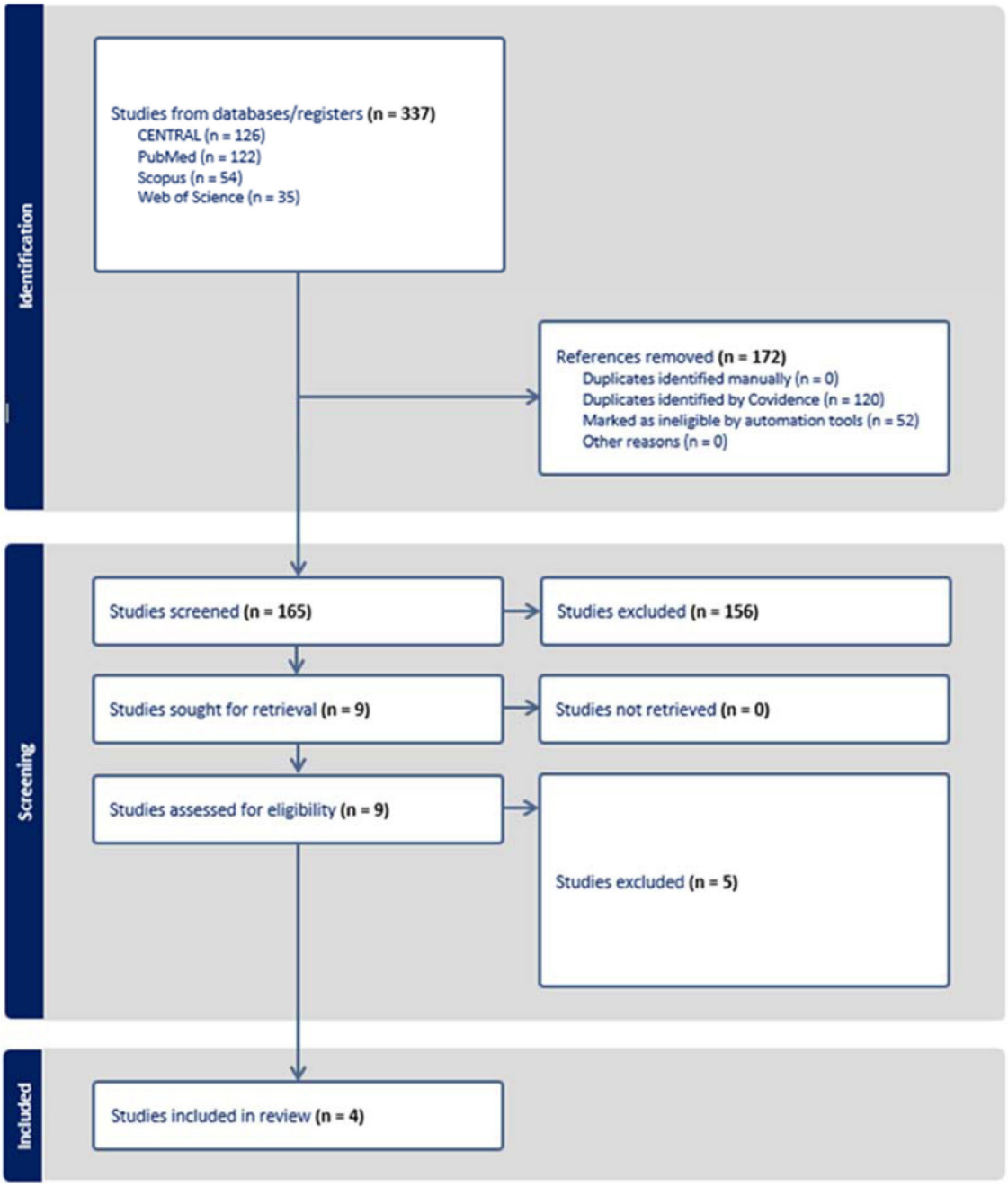

Figure 1. Flow diagram of study screening and selection.
Reasons for exclusion of studies at full-text review (*n* = 5): Ferrer et al., 2003 – Wrong intervention: NIV used as treatment for acute respiratory failure, not as a preoxygenation strategy before intubation; Frat et al., 2017 – Study design: protocol publication only, no outcome data reported; Gibbs et al., 2023 – Study design: protocol and statistical analysis plan only, no outcome data reported (the completed trial [PREOXI, Gibbs et al.[16]] was included separately); Jaber et al.[18] (OPTINIV trial) – Wrong comparator: compared NIV + high-flow nasal oxygen versus NIV alone, without a standard oxygen mask control group; Jaber et al.[18] (Protocol) – Study design: protocol publication for the OPTINIV trial, which did not meet inclusion criteria due to wrong comparator.

Sensitivity analyses

Meta-regression using year of publication as a moderator did not show a significant association with effect size (β = 0.052; 95% CI – 0.059 to 0.163; $p = 0.36$; $R^2 = 0\%$), suggesting that year of publication does not explain between-study variability (Fig. 4).

Egger's regression test did not reveal funnel-plot asymmetry (intercept = −0.19; 95% CI – 7.76 to 7.38; $p = 0.92$) (Fig. 5). Given that only 4 studies were available, this analysis is exploratory and should be interpreted with caution.

Discussion

In critically ill adults undergoing emergency intubation, preoxygenation with NIV did not significantly reduce peri-intubation hypoxemia ($SpO2 < 80\%$) compared with a non–positive-pressure face mask under the HKSJ-adjusted random-effects model (RR 0.39; 95% CI 0.14–1.04; $p = 0.08$). Although the pooled point estimate favored NIV and three of four trials individually demonstrated significant reductions, the combined difference did not reach statistical significance. Safety outcomes showed no statistically significant differences, though the low event

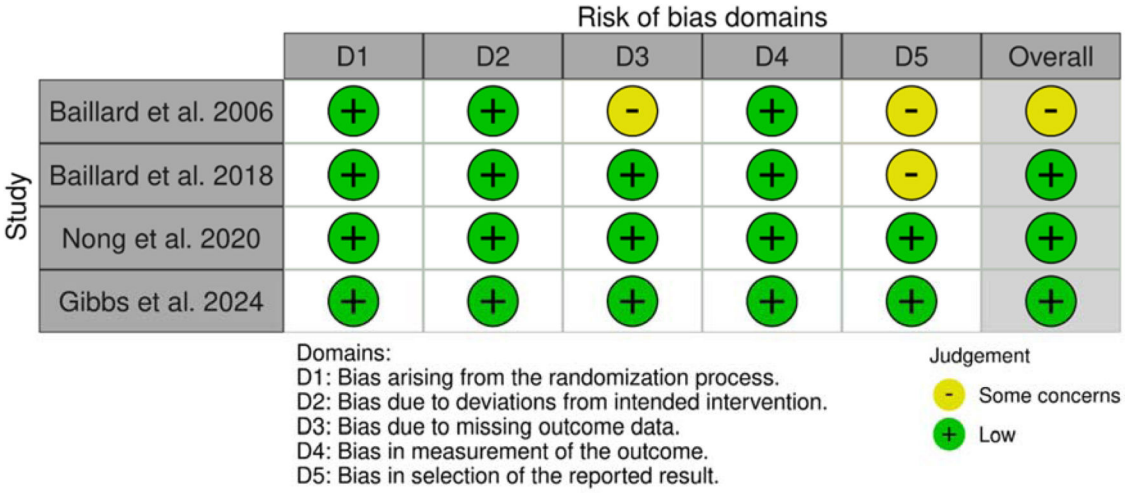

Figure 2. Risk of bias summary - results of ROB2 tool with traffic light plot. Legend: ROB2 - risk of bias 2 tool.

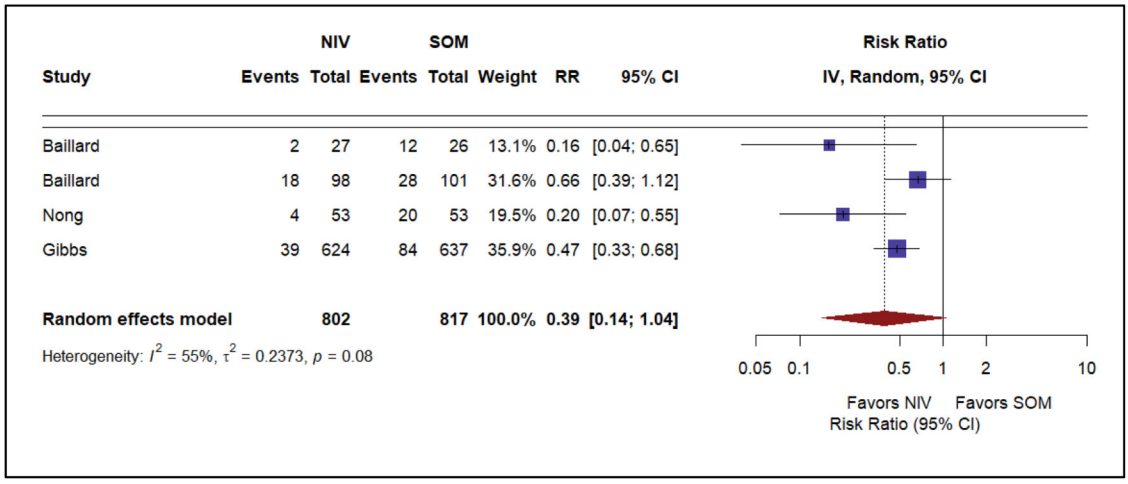

Figure 3. Forest plot for the outcome of peri-intubation severe hypoxemia (SpO_2 <80%), showing a reduced risk with NIV compared to standard oxygen mask (RR 0.39; 95% CI 0.14–1.04; p = 0.08).
Note: NIV – noninvasive ventilation; SOM – standard oxygen mask; CI – confidence interval; IV – inverse variance.

rates limit definitive conclusions. Moderate heterogeneity was observed (I^2 = 55%) with no evidence of relevant funnel plot asymmetry. These findings are concordant with physiological rationale—alveolar recruitment and increased functional residual capacity with positive pressure[39]—and with both recent and earlier trials.

Our meta-analysis provides evidence to answer the question related to hypoxemia, but is insufficient to draw conclusions for rare outcomes, such as aspiration and others. Applicability is high for hospitals equipped with NIV and trained personnel. However, important gaps persist for key subgroups (morbid obesity, pregnancy, severe trauma, prehospital settings) and for head-to-head comparisons with high-flow nasal oxygen (HFNO) in severe hypoxemia, where results have been mixed.[16–22]

Our results align with recent RCTs that demonstrated a reduction in hypoxemia with NIV versus standard face mask and with earlier trials suggesting less desaturation in severe hypoxemia.[16–19] In contrast, previous reviews pooled heterogeneous interventions (e.g., apneic oxygenation, HFNO), making it difficult to attribute the effect specifically to NIV.[24–26] Compared with HFNO, the direct comparative evidence for preoxygenation is less conclusive or dependent on baseline severity, underscoring that NIV offers advantages when effective positive end-expiratory pressure (PEEP) is required before induction.[20–22]

An important consideration when interpreting the present findings is the heterogeneity in the NIV modalities employed across studies. As shown in Table 1, some trials used CPAP alone, others used pressure support ventilation (PSV) with PEEP, and the PREOXI trial allowed operator-selected parameters including both CPAP and bilevel modes. From a physiological standpoint, CPAP provides a constant level of positive airway pressure that promotes alveolar recruitment and increases functional residual capacity, whereas bilevel NIV (PSV with PEEP) adds inspiratory pressure support, which augments tidal volume and may further improve alveolar ventilation and gas exchange. Because no individual trial directly compared CPAP with bilevel NIV for preoxygenation, and because the small number of included studies precluded a meaningful subgroup or sensitivity analysis differentiating these modalities, we did not perform a separate exploratory analysis. Accordingly, our results should be interpreted as reflecting the benefit of applying positive airway pressure during preoxygenation in general, rather than the superiority of any specific NIV mode. This variability is acknowledged as a source of clinical heterogeneity in the Limitations section.

Regarding the role of high-flow nasal oxygen (HFNO) in the current landscape, it is important to contextualize our findings. HFNO has been widely adopted for preoxygenation and can serve as apneic oxygenation during laryngoscopy, as demonstrated in the FLORALI-2 and OPTINIV trials.[18,20] In the studies included in our review, the use of concomitant apneic oxygenation (e.g., nasal cannula during laryngoscopy) was permitted in the PREOXI trial, where operators could provide supplemental

Table 2
Summary of Findings (GRADE). **Population:** Critically ill adults undergoing emergency intubation (ICU/ED). **Intervention:** Preoxygenation with NIV (positive airway pressure; e.g., FiO2 100%, PEEP ≥ 5 cmH2O). **Comparator:** Standard oxygen mask or other non-positive-pressure device.

Outcome (follow-up)	No. of patients (studies)	NIV group	Mask group	Relative effect (95% CI)	Absolute difference (95% CI)	Certainty	Interpretation
Severe hypoxemia (SpO2 < 80%)	1619 (4 RCTs)	63/802 (7.9%)	144/817 (17.6%)	RR 0.39 (0.14–1.04)	107 fewer per 1000 (from 151 fewer to 7 more)	⊕⊕⊕○ Moderate	Point estimate favours NIV, but the pooled difference is not statistically significant under the HKSJ-adjusted model (95% CI crosses unity); 3 of 4 trials individually showed significant reductions.
Aspiration or regurgitation	1555 (3 RCTs)	8/771 (1.0%)	13/784 (1.7%)	RR 0.64 (0.27–1.51)	6 fewer per 1000 (from 12 fewer to 9 more)	⊕⊕○○ Low	No statistically significant difference; very low event rates produce wide confidence intervals, precluding firm conclusions.

Notes: The severe hypoxemia analysis includes all four RCTs reporting the SpO2 < 80% threshold: Baillard 2006 (2/27 vs 12/26), Nong 2020 (4/53 vs 20/53), Baillard 2018 (18/98 vs 28/101), and Gibbs 2024 (39/624 vs 84/637; SpO2 < 80% reported as an exploratory outcome, the trial's primary outcome being SpO2 < 85%). The pooled risk ratio was estimated with a random-effects model (REML) with the Hartung–Knapp–Sidik–Jonkman adjustment; because the 95% confidence interval crosses unity, the pooled difference is not statistically significant, consistent with the main text. The aspiration/regurgitation analysis includes three RCTs (Baillard 2006, Baillard 2018, and Gibbs 2024). Absolute differences were derived from the pooled control-group risk and the corresponding relative effect. GRADE certainty was downgraded one level for imprecision for severe hypoxemia and for very serious imprecision (low event rates) for aspiration.
Abbreviations: NIV, noninvasive ventilation; SpO2, peripheral oxygen saturation; RCT, randomized controlled trial; RR, risk ratio; RD, risk difference; CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; ICU, intensive care unit; ED, emergency department; FiO2, fraction of inspired oxygen; PEEP, positive end-expiratory pressure.
GRADE certainty ratings: ⊕⊕⊕⊕ High = We are very confident that the true effect lies close to that of the estimate; ⊕⊕⊕○ Moderate = We are moderately confident in the effect estimate; ⊕⊕○○ Low = Our confidence in the effect estimate is limited; ⊕○○○ Very low = We have very little confidence in the effect estimate.

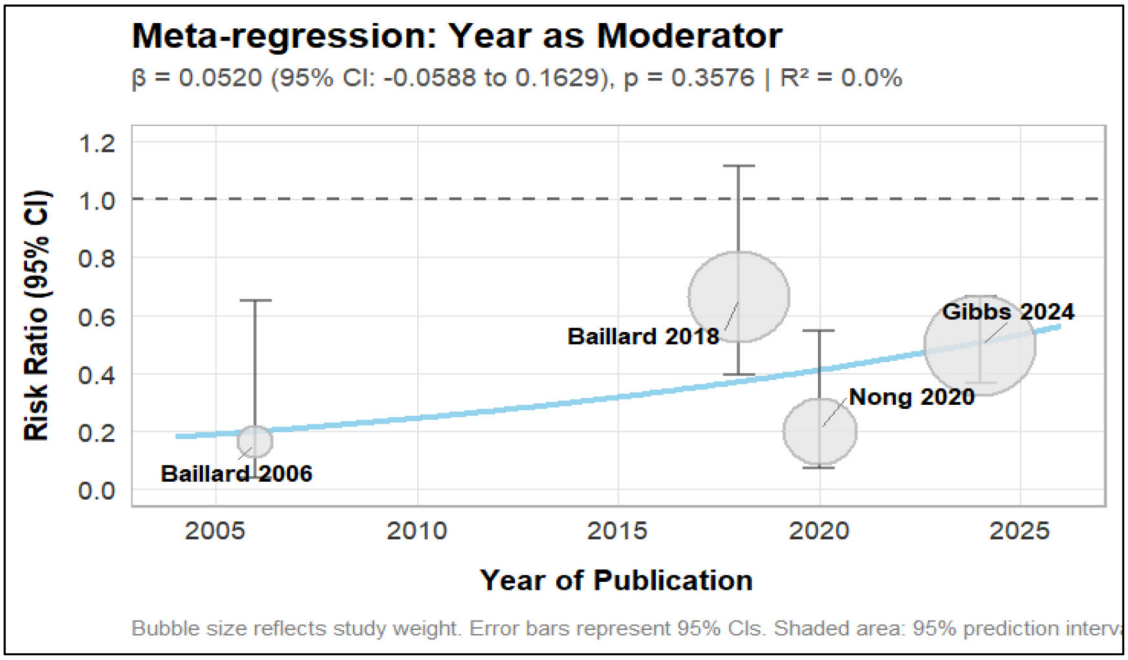

Figure 4. Meta-regression bubble plot for the outcome of peri-intubation hypoxemia, using publication year as a moderator.
Note: No statistically significant relationship was found ($p = 0.36$; $R^2 = 0\%$). Bubble size reflects study weight; error bars represent 95% confidence intervals; shaded area shows the 95% prediction interval.

oxygen through standard nasal cannula or HFNO to patients in either group during the apneic period. In the other three trials (Baillard 2006, Baillard 2018, and Nong 2020), no explicit co-intervention with apneic oxygenation was described. Therefore, in the PREOXI trial, the observed benefit cannot be attributed exclusively to NIV during the preoxygenation phase but may also reflect combined effects of NIV preoxygenation and apneic oxygenation during the apneic interval. Our review specifically addressed the comparison of NIV versus facemask without positive pressure; however, in clinical practice, HFNO represents an increasingly relevant alternative, particularly in patients with moderate-to-severe hy-

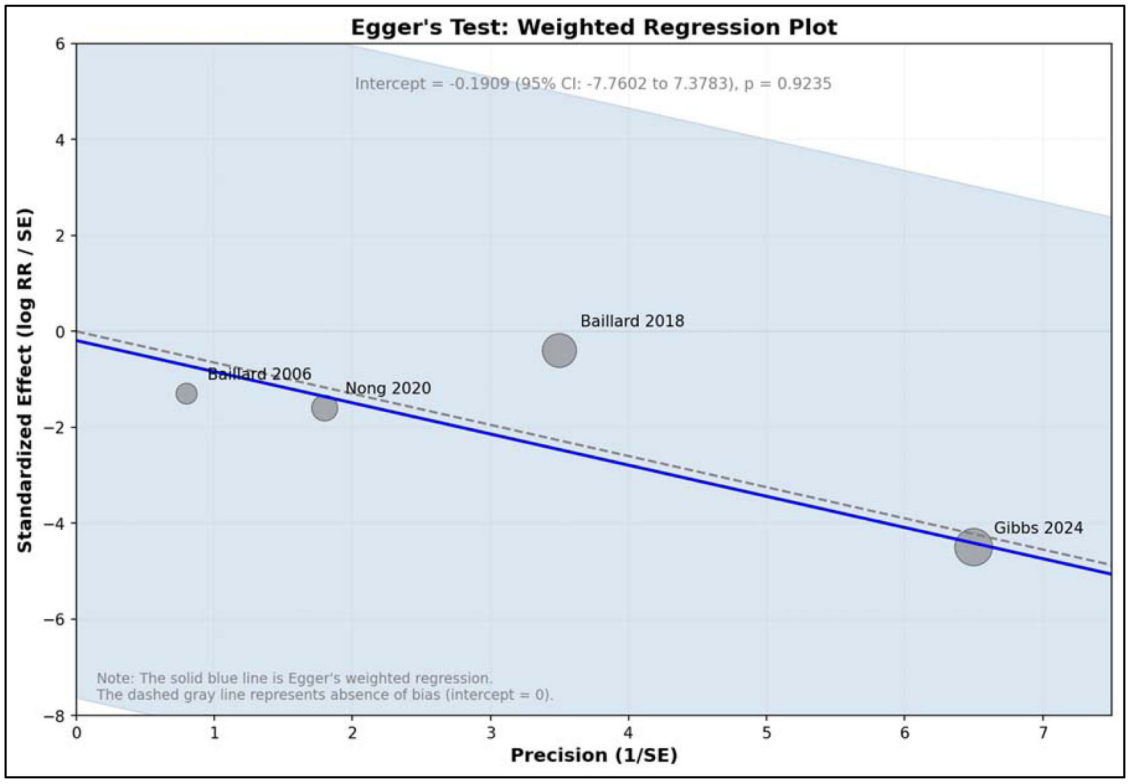

Figure 5. Egger's regression test for funnel plot asymmetry. No statistically significant asymmetry was detected (intercept = −0.19; 95% CI – 7.76 to 7.38; $p = 0.92$), suggesting no evidence of publication bias.
Note: The solid blue line represents Egger's weighted regression; the dashed gray line represents absence of bias (intercept = 0). Given the small number of studies ($n = 4$), this analysis should be interpreted with caution.

poxemia where HFNO may provide adequate oxygenation support with greater patient comfort and the ability to maintain oxygenation during the apneic period without interruption. The direct comparison between NIV and HFNO for preoxygenation in critically ill patients remains an area of active investigation, and the present results do not allow conclusions about the relative superiority of NIV over HFNO.

The variability in the control-group preoxygenation method also deserves consideration. As detailed in Table 1, the standard facemask approach was not uniformly defined across studies: Baillard 2006 and 2018 used a non-rebreather mask with reservoir at 15 L/min of oxygen, Nong 2020 used a standard reservoir mask, and the PREOXI trial allowed local practice to dictate the specific device (non-rebreather mask or bag-mask device without manual ventilation) and flow rate. Furthermore, the duration of preoxygenation was standardized at 3 min in three studies but was left to clinician discretion ("per local practice") in the PREOXI trial, although at least 3 min of preoxygenation was achieved in over 95% of patients in both groups. Given that the efficacy of preoxygenation depends critically on the technique, duration, quality of mask seal, flow rate, and patient cooperation, this variability may represent an additional source of methodological heterogeneity.

Limitations

This review has several limitations. First, the small number of RCTs, mostly with modest sample sizes, limits statistical power for rare outcomes and subgroup analyses. Second, the hypoxemia threshold was not uniform across trials, as the primary outcome of the PREOXI trial used SpO2 < 85%; to enable a single pooled estimate at a common threshold, we used its exploratory SpO2 < 80% data, which may introduce minor outcome-definition heterogeneity. Third, variability in NIV settings (CPAP vs BiPAP, different pressure levels) and co-interventions may contribute to heterogeneity. In particular, the grouping of CPAP and bi-level NIV (pressure support with PEEP) under the umbrella term "NIV" may obscure differences in their physiological effects and represents a relevant source of clinical heterogeneity. Additionally, variability in the control-group method (non-rebreather mask with 15 L/min vs local practice, non-standardized duration in one trial) and in the use of concomitant apneic oxygenation (permitted in the PREOXI trial but not described in the other studies) may further limit the comparability of results across trials. Fourth, the lack of individual patient data precluded exploration of treatment effects in specific subgroups such as patients with severe obesity or acute respiratory distress syndrome. Fifth, limited representation of low- and middle-income countries and prehospital contexts restricts generalizability to these settings. Finally, different NIV devices and interfaces across studies may affect the consistency of the intervention effect.

Conclusion

In critically ill adults requiring emergency tracheal intubation, preoxygenation with NIV did not result in a statistically significant reduction of peri-intubation hypoxemia (SpO2 < 80%) compared with a standard oxygen mask under the HKSJ-adjusted random-effects model (moderate-certainty evidence). The pooled point estimate nonetheless favored NIV, and three of the four individual trials showed significant reductions, suggesting a possible clinically relevant benefit that did not reach statistical significance in the pooled analysis and warrants confirmation in adequately powered trials. Major adverse events were infrequent, and no statistically significant differences were observed for aspiration, though confidence intervals were wide. These findings support consideration of NIV for preoxygenation where equipment and trained personnel are available. However, since the majority of enrolled patients had hypoxemic respiratory failure, the applicability of these results to other clinical profiles such as patients with

severe hemodynamic instability, profound shock, polytrauma, morbid obesity, pregnancy, anticipated difficult airway, or high risk of aspiration remains uncertain. Patients with moderate-to-severe hypoxemia who require alveolar recruitment may derive the greatest benefit from positive-pressure preoxygenation, whereas in scenarios requiring immediate intubation without a temporal margin (e.g., cardiac arrest, massive hemoptysis) or where the risk of gastric distension and aspiration is particularly elevated, NIV may not be the optimal strategy. Therefore, the decision to use NIV for preoxygenation should be individualized according to the clinical context, patient profile, available equipment, and the experience of the treating team. Further research should refine safety estimates for rare outcomes and clarify effects in key subgroups.

CRediT authorship contribution statement

Alvaro Andre Vargas Aguilar (AAVA) contributed to the study conception; Jose Luis Villca Villegas (JLVV) and Sinai Fernanda Claros Rocabado (SFCR) participated in data collection; JLVV performed the statistical analysis; JLVV, SFCR and Gustavo Irusta (G.I.) drafted the initial version of the article, and all authors contributed critically to the writing of the manuscript and approved the final version.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this manuscript, the authors used ChatGPT (OpenAI) exclusively to assist with grammar, spelling and improvement of language clarity. The tool was not used to generate scientific content, analyze data, or write sections containing original ideas or references. All AI-assisted outputs were critically reviewed, verified and edited by the authors, who take full responsibility for the accuracy and integrity of the content, in accordance with the ethical AI use policy of Medicina Intensiva.

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Declaration of competing interest

The authors declare no conflicts of interest regarding the present study.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.medine.2026.502566.

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