



The Indonesian Journal of General Medicine

THE ASSOCIATION BETWEEN THE HIGH-FLOW NASAL CANNULA TECHNIQUE DURING BRONCHOSCOPY AND THE MAINTENANCE OF PERIPHERAL OXYGEN SATURATION (SPO₂): A SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS AND PRIMARY STUDIES

¹ Muhamad Luthfi Asyhar, ² Chaerunnisa Auliya Putu Sugiyarti, ³
Jeremia J.P Munthe, ⁴ Dwi Putri Wijayanti, ⁵ Iman Taufiq, ⁶ Sharon
Meiliana Widjaja, ⁷ Antoinetta Fernanda Sitanggang, ⁸ Novalia Amelinda,
⁹ Vina Rahmatika

¹ Waras Wiris Regional General Hospital, Indonesia / Graduate of Faculty of
Medicine, Airlangga University, Indonesia

² dr Soeratno Gemolong Regional General Hospital, Indonesia / Graduate of
Faculty of Medicine, Muhammadiyah University of Yogyakarta, Indonesia

³ Sidikalang Regional General Hospital, Indonesia / Graduate of Faculty of
Medicine, North Sumatera University, Indonesia

⁴ Muhammadiyah Kaliwungu Kendal Regional General Hospital, Indonesia /
Graduate of Faculty of Medicine, Sultan Agung Islamic University, Semarang,
Indonesia

⁵ KH. Daud Arif Kuala Tungkal Regional General Hospital, Indonesia /
Graduate of Faculty of Medicine, University of Jambi, Indonesia

⁶ Dr. Moewardi Regional General Hospital, Indonesia / Graduate of Faculty of
Medicine, Maranatha Christian University, Indonesia

⁷ Ngimbang Lamongan Regional General Hospital, Indonesia / Graduate of
Faculty of Medicine, Widya Mandala Catholic University, Indonesia

⁸ Bukit Menoreh Regional General Hospital, Indonesia / Graduate of Faculty of
Medicine, Sultan Agung Islamic University, Semarang, Indonesia

⁹ Al-Irsyad General Hospital, Surabaya, Indonesia / Graduate of Faculty of
Medicine, Muhammadiyah University of Surabaya, Indonesia, Indonesia

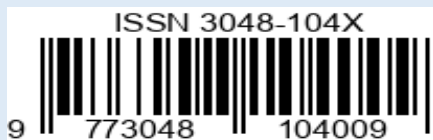
Corresponding Email : muhamadluthfiasyhar@yahoo.com

Article History :

Received date : 2026/07/04
Revised date : 2026/08/21
Accepted date : 2026/09/17
Published date : 2026/10/04



Copyright: © 2024 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (BY NC) license (<https://creativecommons.org/licenses/by-nc/4.0/>).



ABSTRACT

Introduction: Peri-procedural hypoxaemia is the most frequent physiological complication of flexible bronchoscopy and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA), particularly under procedural sedation, bronchoalveolar lavage (BAL) and in patients with limited respiratory reserve. High-flow nasal cannula (HFNC) delivers heated, humidified gas at up to 60–80 L/min with a stable fraction of inspired oxygen (FiO₂), nasopharyngeal dead-space washout and a flow-dependent positive airway pressure. We aimed to quantify the association between HFNC use during bronchoscopy and the maintenance of peripheral oxygen saturation (SpO₂), with emphasis on evidence published in the last 15 years.^{1–3}

Methods: The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines. Randomised controlled trials (RCTs), cohort, case–control, cross-sectional and other prospective or retrospective observational studies comparing HFNC with conventional oxygen therapy (COT), non-invasive ventilation (NIV) or different HFNC flows during bronchoscopy were eligible.^{4–6}

Results: Thirty-two primary studies (23 RCTs and 9 observational/non-randomised studies; 4,572 participants; 2012–2026) were included. In 12 adult RCTs (2,318 participants), HFNC reduced intraprocedural desaturation (SpO₂ < 90%) from 39.9% to 15.0% (risk ratio [RR] 0.34, 95% CI 0.25–0.47; I² = 72%; prediction interval 0.12–0.95),

corresponding to 262 fewer events per 1,000 patients and a number needed to treat of 3.8. Including the PROSA-2 trial and two observational studies (odds ratio 0.20, 95% CI 0.14–0.28) did not change the inference. HFNC increased nadir SpO₂ by 4.95 percentage points (95% CI 2.89–7.00; five RCTs), reduced procedure interruption (RR 0.39, 0.28–0.54; I² = 13%), airway manoeuvres or support escalation (RR 0.40, 0.24–0.67) and severe hypoxaemia/advanced rescue (RR 0.31, 0.16–0.63). A monotonic flow–response relationship was observed, with a reported ED₅₀ of approximately 43 L/min. In moderate-to-severe hypoxaemic respiratory failure, NIV provided better oxygenation than HFNC. The effect was robust across all sensitivity analyses; certainty was moderate for desaturation and procedure interruption.^{7–13}

Discussion: The benefit of HFNC was consistent in direction across sedation depth, procedure type (EBUS-TBNA vs. non-EBUS bronchoscopy), baseline risk and comparator device, although heterogeneity in magnitude was substantial and was driven chiefly by trials with matched nominal FiO₂ or very high control-arm risk. Neutral trials under conscious sedation and matched FiO₂ suggest that part of the benefit derives from superior and more stable oxygen delivery, while physiological studies support additional contributions from preserved end-expiratory lung volume and dead-space washout.^{14–}

16

Conclusion: HFNC during bronchoscopy is associated with clinically meaningful preservation of

SpO₂, fewer hypoxaemic events and fewer procedure interruptions, with moderate certainty. HFNC at $\geq$ 45–60 L/min should be preferred for sedated, prolonged or BAL-containing procedures and for patients at increased risk, whereas NIV/CPAP remains preferable in established moderate-to-severe hypoxaemic respiratory failure. Adequately powered, blinded-outcome multicentre trials with standardised desaturation definitions and patient-important endpoints are required.^{2,17}

Keywords: high-flow nasal cannula; high-flow nasal oxygen; flexible bronchoscopy; endobronchial ultrasound; oxygen saturation; hypoxaemia; procedural sedation; meta-analysis.⁴

INTRODUCTION

Background

Flexible bronchoscopy is a cornerstone of contemporary respiratory medicine, providing airway inspection, BAL, bronchial brushing and biopsy, transbronchial lung biopsy (TBLB), cryobiopsy and, through EBUS-TBNA, minimally invasive mediastinal staging. The British Thoracic Society (BTS) guideline recommends continuous pulse oximetry for all patients and supplemental oxygen when SpO₂ falls by more than 4% or below 90% for more than one minute, recognising hypoxaemia as the most common and most modifiable physiological complication of the procedure.^{1,18}

The case-mix of bronchoscopy has shifted toward older patients with chronic obstructive pulmonary disease (COPD), obesity and obstructive sleep apnoea (OSA), interstitial lung disease, lung transplantation and malignant central airway obstruction, while procedures have become longer and more complex. Concurrently, sedation practice has intensified: most international guidelines now recommend offering sedation, and propofol-based deep sedation administered by anaesthesiologists is increasingly used, particularly for EBUS-TBNA. Both trends amplify the risk of desaturation, hypercapnia and airway obstruction, yet recommendations on the optimal oxygen-delivery interface remain heterogeneous.^{10,19,20}

Desaturation is not merely a monitoring artefact. In a retrospective cohort of 569 patients, a nadir SpO₂ ≤ 94% during bronchoscopy was independently associated with post-bronchoscopy respiratory adverse events (adjusted odds ratio 3.16), especially among older patients, current smokers and those with COPD or decompensated heart failure. Hypoxaemia also forces procedure interruptions, prolongs scope time, lowers diagnostic yield when BAL or sampling must be curtailed and triggers airway rescue manoeuvres.^{8,9,21}

Conventional low-flow oxygen (nasal prongs at 2–6 L/min, face masks, bite-block or nasopharyngeal delivery) provides an FiO₂ that varies with minute ventilation and mouth breathing and is readily diluted by room-air entrainment when the peak inspiratory flow exceeds the delivered flow. Non-invasive ventilation and continuous positive airway pressure (CPAP) improve oxygenation in severe hypoxaemia but require a sealed interface, specialised equipment and expertise, and may hamper bronchoscope manipulation.^{2,17,22}

Pathophysiological Rationale for HFNC During Bronchoscopy

The mechanisms of peri-bronchoscopic hypoxaemia and the corresponding physiological countermeasures of HFNC are summarised in Figure 1. The bronchoscope

occupies a substantial proportion of the tracheal lumen, increasing airway resistance and the work of breathing; repeated suction de-recruits alveoli and reduces end-expiratory lung volume (EELV); instilled saline and lidocaine widen ventilation–perfusion ($\dot{V}/\dot{Q}$) mismatch; and sedative–opioid combinations depress respiratory drive and promote upper-airway collapse.^{8,16,23}

HFNC counteracts these processes through several flow-dependent mechanisms. When delivered flow approaches or exceeds peak inspiratory flow, FiO_2 becomes stable and predictable; nasopharyngeal dead space is flushed with fresh gas, improving the efficiency of alveolar ventilation; and a modest positive airway pressure (typically 1–7 cmH₂O, higher with the mouth closed) helps preserve EELV. Heating and humidification maintain mucociliary function and improve tolerance. In healthy volunteers, HFNC at 40–60 L/min reduced respiratory rate and calculated dead-space ventilation, and electrical impedance tomography during BAL showed that HFNC prevented the fall in EELV observed with standard therapy.^{3,16,24–27}

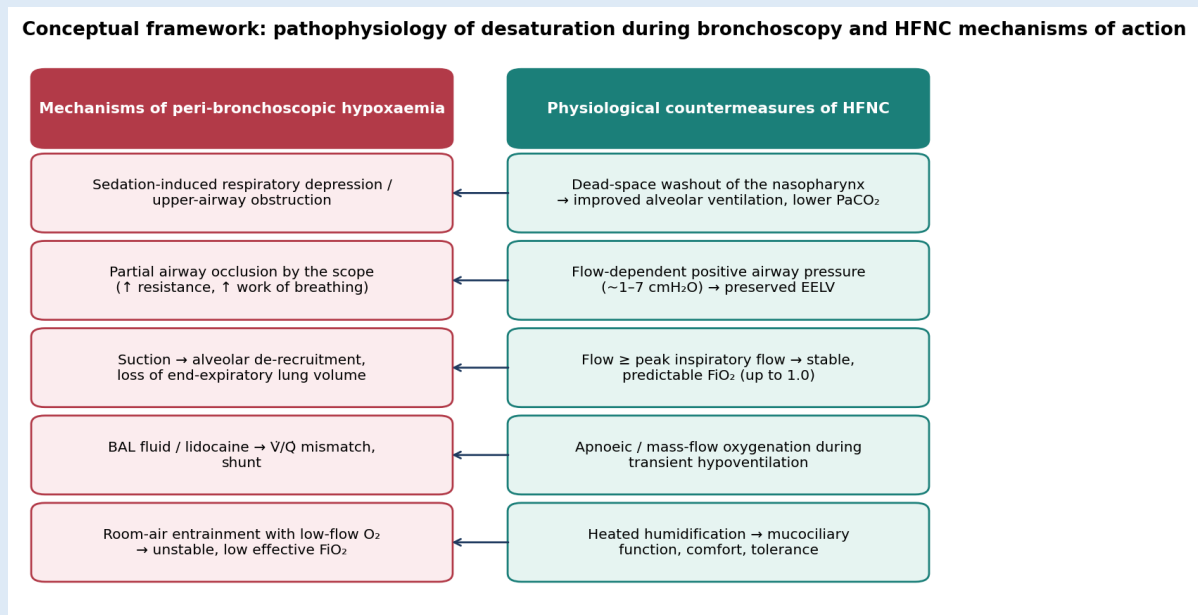


Figure 1. Conceptual framework linking the principal mechanisms of peri-bronchoscopic hypoxaemia (left) with the physiological countermeasures of high-flow nasal cannula (right). EELV, end-expiratory lung volume; $\dot{V}/\dot{Q}$, ventilation–perfusion ratio. Constructed by the authors from physiological and clinical sources.^{3,23,24,26,28}

Research Gap

Several meta-analyses published between 2021 and 2026 have consistently reported fewer hypoxaemic events with HFNC. However, they (i) restricted inclusion to RCTs and therefore ignored the growing body of prospective and retrospective clinical data, including

high-risk and hypoxaemic populations; (ii) frequently mixed comparators (low-flow devices and NIV) or procedures (gastrointestinal endoscopy); (iii) rarely quantified absolute effects, prediction intervals or the numbers needed to treat; (iv) did not model the flow–response relationship; and (v) did not incorporate the most recent large trials published in 2025–2026, including PROSA-2 in COPD, the HIFLO-EBUS trial, a four-arm deep-sedation flow trial, a matched-FiO₂ multicentre EBUS trial and the first trial targeting patient-important escalation outcomes in acute respiratory failure (ARF).^{10,15,29–38}

It also remains unclear whether the benefit of HFNC depends on sedation depth, procedure type, baseline risk, the comparator device or the delivered flow, and where the boundary lies between HFNC and NIV in patients with pre-existing hypoxaemia. These uncertainties translate into heterogeneous practice, as reflected by the international OxyFOB observational programme designed specifically to describe real-world oxygenation strategies during bronchoscopy.^{17,19,39}

Novelty

This review is, to our knowledge, the first to (i) integrate RCTs with prospective and retrospective primary studies under a unified design-stratified framework assessed with RoB 2 and ROBINS-I; (ii) include the complete 2025–2026 generation of trials; (iii) report prediction intervals, Hartung–Knapp and Paule–Mandel sensitivity models, cumulative and leave-one-out meta-analysis, a meta-regression on control-arm risk and a L'Abbé analysis; (iv) model the flow–response curve from arm-level data; (v) translate relative effects into absolute effects across a spectrum of baseline risks; and (vi) derive an evidence-informed clinical pathway applicable to both high-resource and resource-constrained bronchoscopy units.^{4–6,11}

Objectives

General objective: to evaluate comprehensively the association between the use of HFNC during bronchoscopy and the maintenance of SpO₂ in patients undergoing diagnostic or interventional bronchoscopic procedures.¹

Specific objectives: (1) to estimate the effect of HFNC versus COT on the incidence of intraprocedural desaturation (primary outcome); (2) to estimate its effect on nadir SpO₂, procedure interruption, airway manoeuvres and escalation of respiratory support, and severe hypoxaemia requiring advanced rescue; (3) to explore effect modification by sedation depth, procedure type, patient risk profile and comparator device; (4) to describe the flow–response relationship; (5) to compare HFNC with NIV in hypoxaemic patients; and (6) to grade the certainty of evidence and derive practice recommendations.^{5,40}

Hypotheses

Primary hypothesis (H₁): compared with conventional low-flow oxygen, HFNC during bronchoscopy reduces the risk of intraprocedural desaturation (SpO₂ < 90%); **null hypothesis (H₀):** the pooled risk ratio equals 1. **Secondary hypotheses:** HFNC increases nadir SpO₂ and reduces procedure interruptions and rescue interventions; the benefit is flow-dependent; and HFNC is not superior to NIV in patients with established moderate-to-severe hypoxaemia.^{11–13}

Significance and Benefits of the Study

Clinical benefit: the review provides quantitative estimates (relative and absolute effects, numbers needed to treat) that allow bronchoscopists, anaesthesiologists and intensivists to select an oxygenation strategy according to individual risk. **Academic benefit:** it clarifies sources of heterogeneity and defines methodological standards for future trials (outcome definitions, blinding of outcome assessment, reporting of arm-level data). **Health-system benefit:** by quantifying reductions in interruptions and airway rescue, the findings inform equipment procurement, sedation-service design and training, including in middle-income settings such as Indonesia where bronchoscopy services and procedural sedation are rapidly expanding.^{19,39}

METHODS

Protocol and Reporting Standard

The review was conducted and reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 statement. Eligibility criteria, outcomes and the analytic plan were specified before data extraction.⁴

Eligibility Criteria

Eligibility was defined using the PICOS framework (Table 1). Only primary studies were eligible for the evidence base. Systematic reviews and meta-analyses were not entered into the characteristics tables or quantitative synthesis but were retrieved to cross-check completeness and to contextualise the findings in the Discussion.⁴

Table 1. Eligibility criteria according to the PICOS framework.

Element	Inclusion criteria	Exclusion criteria
Population	Patients of any age undergoing flexible bronchoscopy (diagnostic or therapeutic), EBUS-TBNA, BAL, TBLB, cryobiopsy or rigid bronchoscopy with spontaneous or apnoeic oxygenation	Procedures other than bronchoscopy (gastrointestinal endoscopy, EUS, radiofrequency ablation, intubation/extubation); animal or bench studies
Intervention	Heated humidified high-flow nasal cannula/high-flow nasal oxygen (any device; standard or single-prong interface)	Nasal CPAP, novel low-flow cannulae or supraglottic devices without high-flow delivery

Comparator	Conventional oxygen therapy (nasal prongs, face mask, bite-block, nasopharyngeal tube), NIV/CPAP, different HFNC flow rates, historical or concurrent controls	Studies without extractable SpO ₂ -related outcome
Outcomes	Primary: incidence of desaturation (SpO ₂ < 90%, or trial-specific threshold). Secondary: nadir SpO ₂ , change in SpO ₂ , procedure interruption, airway manoeuvres/escalation, severe hypoxaemia/advanced rescue, PaO ₂ , CO ₂ , comfort, complications	—
Study design	RCTs (parallel or multi-arm), quasi-randomised trials, prospective/retrospective cohorts, case-control, cross-sectional and other observational designs (including case series with ≥ 10 patients)	Systematic reviews/meta-analyses (discussion only), narrative reviews, protocols, editorials, single case reports, conference abstracts without full report
Time frame and language	Published January 2011 – September 2026 (last 15 years); English-language full text or structured abstract with extractable data	Publications before 2011

BAL, bronchoalveolar lavage; CPAP, continuous positive airway pressure; EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration; EUS, endoscopic ultrasound; NIV, non-invasive ventilation; TBLB, transbronchial lung biopsy.

Search Strategy

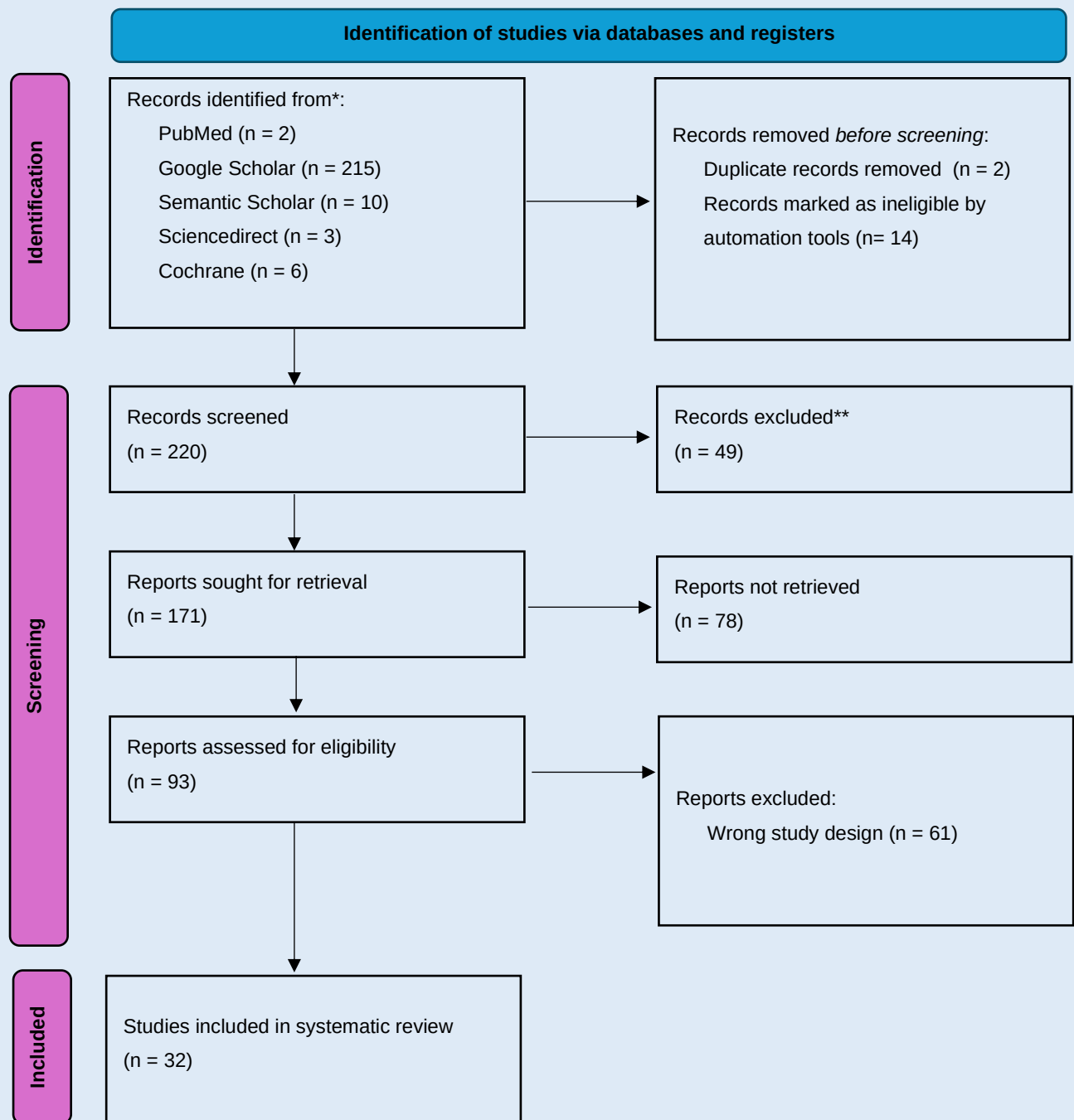
The keywords used for this research based PICO :

PICO Element	Keyword 1	Keyword 2	Keyword 3
P (Population)	Patients undergoing bronchoscopy	Adults undergoing flexible bronchoscopy	Patients with hypoxaemia during bronchoscopy
I (Intervention)	High-flow nasal cannula	High-flow nasal oxygen therapy	Heated humidified high-flow oxygen
C (Comparison)	Conventional oxygen therapy	Low-flow nasal cannula or face mask	Non-invasive ventilation
O (Outcome)	Peripheral oxygen saturation	Intraprocedural desaturation	Procedure interruption and rescue

The Boolean MeSH keywords inputted on databases for this research are: ("Patients undergoing bronchoscopy" OR "Adults undergoing flexible bronchoscopy" OR "Patients with hypoxaemia during bronchoscopy") AND ("High-flow nasal cannula" OR "High-flow nasal oxygen therapy" OR "Heated humidified high-flow oxygen") AND ("Conventional oxygen therapy" OR "Low-flow nasal cannula or face mask" OR "Non-invasive ventilation") AND ("Peripheral oxygen saturation" OR "Intraprocedural desaturation" OR "Procedure interruption and rescue")

Article Search Strategy

Database	Keywords	Hits
Pubmed	<i>("Patients undergoing bronchoscopy" OR "Adults undergoing flexible bronchoscopy" OR "Patients with hypoxaemia during bronchoscopy") AND ("High-flow nasal cannula" OR "High-flow nasal oxygen therapy" OR "Heated humidified high-flow oxygen") AND ("Conventional oxygen therapy" OR "Low-flow nasal cannula or face mask" OR "Non-invasive ventilation") AND ("Peripheral oxygen saturation" OR "Intraprocedural desaturation" OR "Procedure interruption and rescue")</i>	2
Google Scholar	<i>("Patients undergoing bronchoscopy" OR "Adults undergoing flexible bronchoscopy" OR "Patients with hypoxaemia during bronchoscopy") AND ("High-flow nasal cannula" OR "High-flow nasal oxygen therapy" OR "Heated humidified high-flow oxygen") AND ("Conventional oxygen therapy" OR "Low-flow nasal cannula or face mask" OR "Non-invasive ventilation") AND ("Peripheral oxygen saturation" OR "Intraprocedural desaturation" OR "Procedure interruption and rescue")</i>	215
Semantic Scholar	<i>("Patients undergoing bronchoscopy" OR "Adults undergoing flexible bronchoscopy" OR "Patients with hypoxaemia during bronchoscopy") AND ("High-flow nasal cannula" OR "High-flow nasal oxygen therapy" OR "Heated humidified high-flow oxygen") AND ("Conventional oxygen therapy" OR "Low-flow nasal cannula or face mask" OR "Non-invasive ventilation") AND ("Peripheral oxygen saturation" OR "Intraprocedural desaturation" OR "Procedure interruption and rescue")</i>	10
Science-direct	<i>("Patients undergoing bronchoscopy") AND ("High-flow nasal cannula") AND ("Peripheral oxygen saturation" OR "Intraprocedural desaturation" OR "Procedure interruption and rescue")</i>	3
Cochrane	<i>("Patients undergoing bronchoscopy" AND "High-flow nasal cannula" AND "Peripheral oxygen saturation" OR "Intraprocedural desaturation" OR "Procedure interruption and rescue")</i>	6



Article search flowchart

Study Selection

Titles and abstracts were screened against the PICOS criteria, followed by full-text assessment of potentially eligible reports. Multiple reports of the same trial (for example, a congress abstract and the full publication) were linked and counted once, with data taken preferentially from the most complete peer-reviewed report. Disagreements in judgement were resolved by re-examination of the source document against predefined criteria. The selection process is presented in the PRISMA 2020 flow diagram in the Results.^{4,41}

Data Collection and Data Items

A standardised extraction form captured bibliographic data, country, design, setting, population and risk profile, sample size per arm, age, procedure, route (oral vs. nasal), sedation/anaesthesia regimen, HFNC device, flow and FiO₂, comparator settings, desaturation definition (threshold and minimum duration), event counts, nadir SpO₂ (mean $\pm$ SD or median [IQR]), procedure interruptions, rescue manoeuvres, escalation of respiratory support, gas-exchange and CO₂ variables, comfort, procedure duration and complications (Table 3). Where only percentages were reported, event counts were back-calculated and verified against the reported percentage and group size.^{8,9,42}

Table 2. Outcome definitions and data items.

Outcome	Operational definition used in this review	Effect measure
Desaturation (primary)	Proportion of patients with ≥ 1 episode of SpO ₂ < 90% ($\leq 90\%$ for > 10 s, < 90% ≥ 30 s, or as defined by the trial) during the procedure	RR (random effects); OR (generic inverse variance) in sensitivity analysis
Nadir SpO ₂	Lowest SpO ₂ recorded between scope insertion and removal	MD (percentage points)
Procedure interruption	Temporary withdrawal or discontinuation of the bronchoscope because of hypoxaemia	RR
Airway manoeuvres / escalation	Jaw thrust, airway adjunct, any predefined intervention, or escalation of oxygen/respiratory support	RR
Severe hypoxaemia / advanced rescue	Severe desaturation (SpO ₂ < 75% or 75–89% > 60 s), bag-mask ventilation, or intubation within 24 h	RR
Other physiological outcomes	PaO ₂ , PaO ₂ /FiO ₂ , PaCO ₂ , EtCO ₂ /PtcCO ₂ , EELI, diaphragm thickening, respiratory rate	Narrative / tabular
Patient-centred and procedural	Comfort, satisfaction, procedure duration, pneumothorax, arrhythmia, agitation	Narrative / tabular

EELI, end-expiratory lung impedance; EtCO₂, end-tidal CO₂; MD, mean difference; OR, odds ratio; PtcCO₂, transcutaneous CO₂; RR, risk ratio.

Risk of Bias Assessment

Risk of bias of RCTs was assessed for the primary oxygenation outcome with the revised Cochrane RoB 2 tool across five domains: randomisation process, deviations from intended interventions (effect of assignment), missing outcome data, measurement of the outcome and selection of the reported result, with an overall judgement of low risk, some concerns or high risk. Because the intervention cannot be blinded to clinicians, domain 2 was rated "some concerns" when rescue manoeuvres, FiO₂ titration or flow adjustments were at the discretion of unblinded staff; domain 4 was rated low when SpO₂ was captured by continuous automated oximetry and "some concerns" when events were recorded manually by unblinded observers or when definitions were unreported.^{5,43}

Non-randomised and observational studies were assessed with ROBINS-I across seven domains (confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes and selection of the reported result), rated low, moderate, serious or critical. Uncontrolled series were rated critical for confounding with respect to comparative inference. Judgements were based on the accessible published reports; when methodological information was unavailable, the more conservative category was assigned.^{6,40}

Table 3. Risk-of-bias judgements for randomised controlled trials (RoB 2, primary oxygenation outcome).

Study	D1	D2	D3	D4	D5	Overall	Principal rationale
Lucangelo 2012 ⁴⁴	Some	Low	Low	Low	Some	Some	Allocation method briefly reported; no registration; ABG objective
Simon 2014 ¹²	Low	Low	Low	Low	Low	Low	Registered (NCT01870765); objective oximetry/ABG
Douglas 2018 ⁷	Low	Some	Low	Low	Low	Some	Flow titrated 30–70 L/min by unblinded anaesthetist; ITT and PP reported
Saksitthichok 2019 ¹³	Low	Low	Low	Low	Some	Some	Registration not verifiable in accessible report
Ben-Menachem 2020 ⁴²	Low	Low	Low	Low	Low	Low	Patient and bronchoscopist blinded to allocation
Yilmazel Ucar 2021 ⁴¹	Some	Some	Low	Some	Some	Some	Randomisation method and desaturation definition not detailed
Irfan 2021 ⁴⁵	Low	Low	Low	Low	Some	Some	Small single-centre trial; objective continuous oximetry
Wang R 2021 ⁸	Low	Some	Low	Some	Low	Some	Sealed envelopes; 24/812 post-randomisation exclusions; SpO ₂ recorded on paper CRF by unblinded collectors
Sharluyan 2021 ⁴⁶	Low	Some	Low	Low	Some	Some	Open-label paediatric trial; ITT analysis
Longhini 2022 ¹⁶	Low	Low	Low	Low	Low	Low	Registered (NCT04016480); ABG and EIT objective
Zhang W 2022 ⁴⁷	Low	Some	Low	Low	Low	Some	Jaw thrust at discretion of unblinded anaesthetist
Freund 2024 ⁴⁸	Some	Some	Some	Low	Some	Some	Block randomisation; one HFNC patient not analysed
Kim HJ 2024 ⁴⁹	Low	Low	Low	Low	Some	Some	General anaesthesia with standardised apnoea protocol
Zhang W 2024 ¹¹	Low	Low	Low	Low	Low	Low	Registered (NCT05298319); six parallel flow arms
Qin 2025 ⁹	Low	Some	Some	Low	Low	Some	Six withdrawals after enrolment; FiO ₂ -matched design

Darje 2025 ¹⁰	Low	Low	Low	Low	Low	Low	Large trial; continuous recording of cumulative hypoxaemia time
Burton 2025 ¹⁴	Low	Low	Low	Low	Low	Low	Registered (ANZCTR); device-captured oxygenation
Sehgal 2025 ³⁶	Low	Some	Low	Low	Low	Some	Open-label; objective oximetry
Gupta 2025 ⁵⁰	Some	Some	Low	Some	Some	High	Non-standard desaturation definition (3% fall); multiple unclear domains
Yue 2025 ⁵¹	Low	Some	Low	Low	Low	Some	Registered (ChiCTR2400085320); rescue at clinician discretion
Rozman 2026 ¹⁵	Low	Low	Some	Low	Low	Some	6 of 126 randomised patients not analysed
Wang M 2026 ³⁷	Low	Some	Some	Low	Low	Some	Four-arm design; 10 of 340 not analysed
Wang R 2026 ³⁸	Low	Some	Low	Some	Low	Some	Escalation decisions by unblinded clinicians despite predefined criteria

D1 randomisation process; D2 deviations from intended interventions; D3 missing outcome data; D4 measurement of the outcome; D5 selection of the reported result. "Some" = some concerns. ABG, arterial blood gas; CRF, case report form; EIT, electrical impedance tomography; ITT, intention-to-treat; PP, per-protocol.

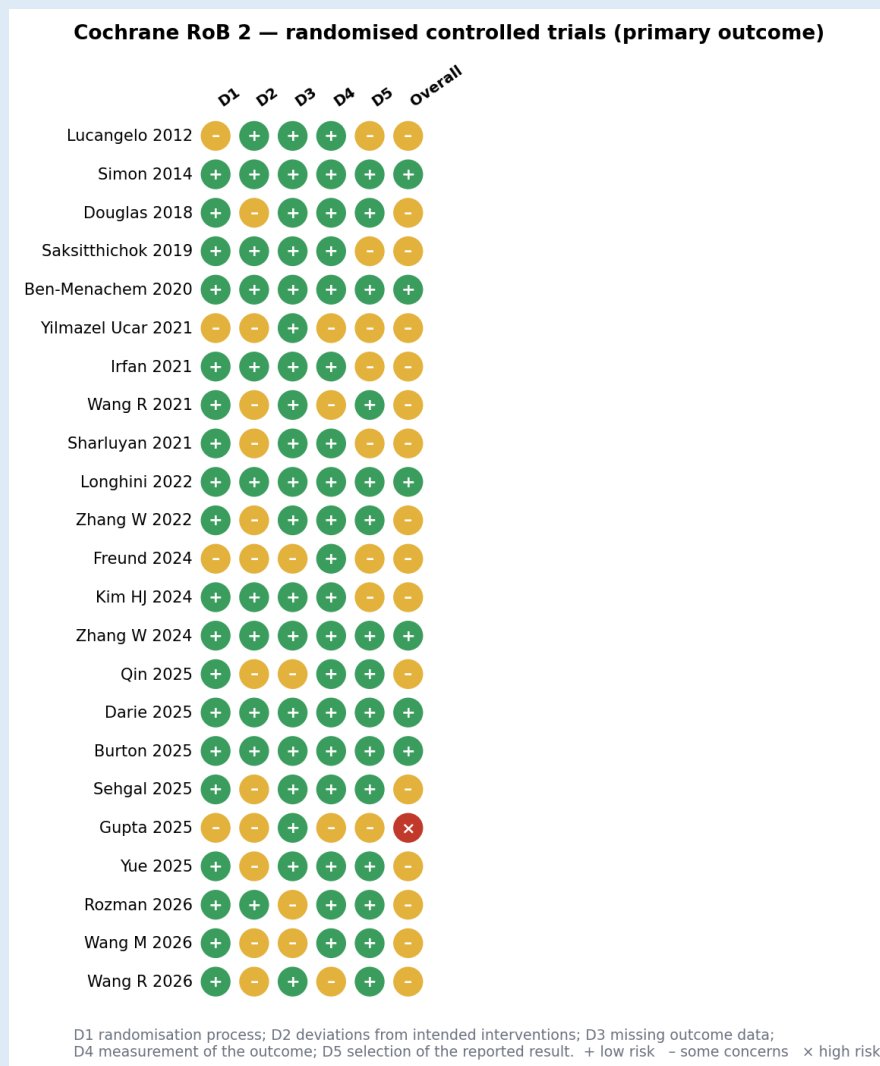


Figure 2. Traffic-light plot of RoB 2 domain-level and overall judgements for the 23 randomised controlled trials.⁵

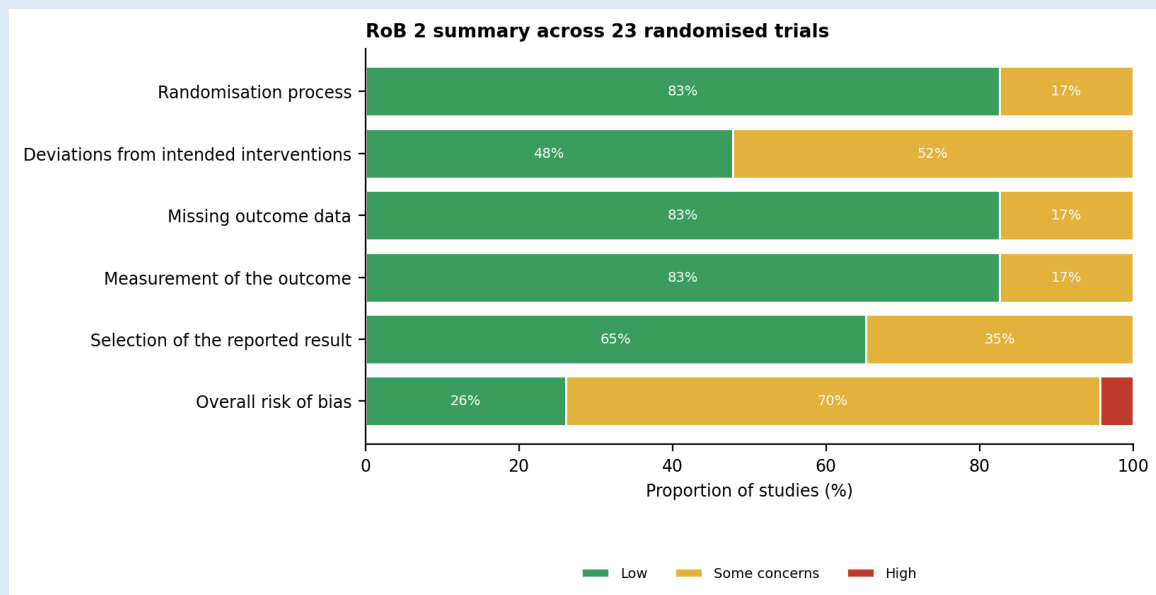


Figure 3. Weighted summary of RoB 2 judgements across domains (proportion of trials). Seven trials (30%) were at low overall risk, 15 (65%) raised some concerns and one (4%) was at high risk; concerns were concentrated in deviations from intended interventions and outcome measurement, reflecting the unavoidable open-label delivery of HFNC.^{5,43}

Table 4. Risk-of-bias judgements for non-randomised and observational studies (ROBINS-I).

Study	D1	D2	D3	D4	D5	D6	D7	Overall	Rationale
Takakuwa 2018 ⁵²	Serious	Mod	Low	Low	Low	Mod	Mod	Serious	Historical control group
Kim EJ 2018 ⁵³	Serious	Mod	Low	Low	Mod	Mod	Mod	Serious	Retrospective; baseline P/F differed between groups
Chung 2018 ⁵⁴	Critical	Serious	Low	Low	Mod	Mod	Mod	Critical	Uncontrolled retrospective series (n = 10)
Service 2019 ⁵⁵	Critical	Mod	Low	Low	Low	Mod	Mod	Critical	Single-arm feasibility cohort
Nilushi 2022 ⁵⁶	Mod	Mod	Low	Low	Low	Mod	Mod	Mod	Sequential allocation; multivariable adjustment
Arias-Sánchez 2023 ⁵⁷	Serious	Mod	Low	Low	Low	Low	Mod	Serious	Allocation by device availability
Ravi 2023 ⁵⁸	Mod	Mod	Low	Low	Low	Mod	Mod	Mod	Quasi-randomised pilot; SAD comparator
Luo 2024 ⁵⁹	Serious	Mod	Low	Low	Low	Mod	Low	Serious	Retrospective; confounding by indication
de Vico 2025 ⁶⁰	Serious	Low	Low	Low	Low	Low	Mod	Serious	Consecutive ASA III patients; non-random allocation

D1 confounding; D2 selection of participants; D3 classification of interventions; D4 deviations from intended interventions; D5 missing data; D6 measurement of outcomes; D7 selection of reported result. Mod, moderate; SAD, supraglottic airway device; P/F, PaO₂/FiO₂ ratio.

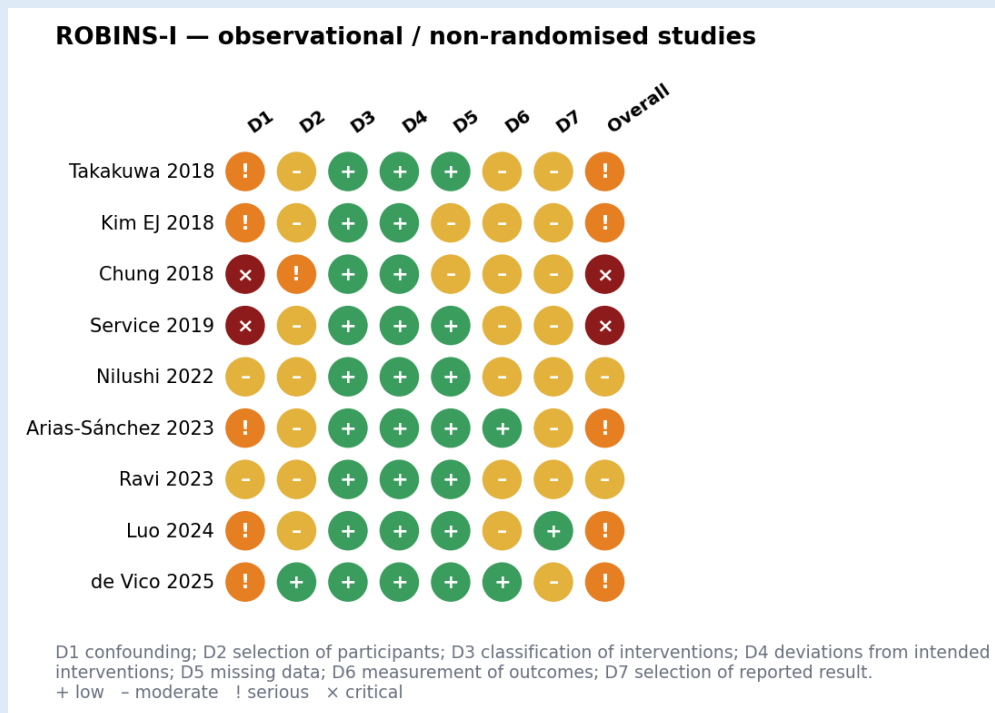


Figure 4. Traffic-light plot of ROBINS-I judgements for the nine observational/non-randomised studies.⁶

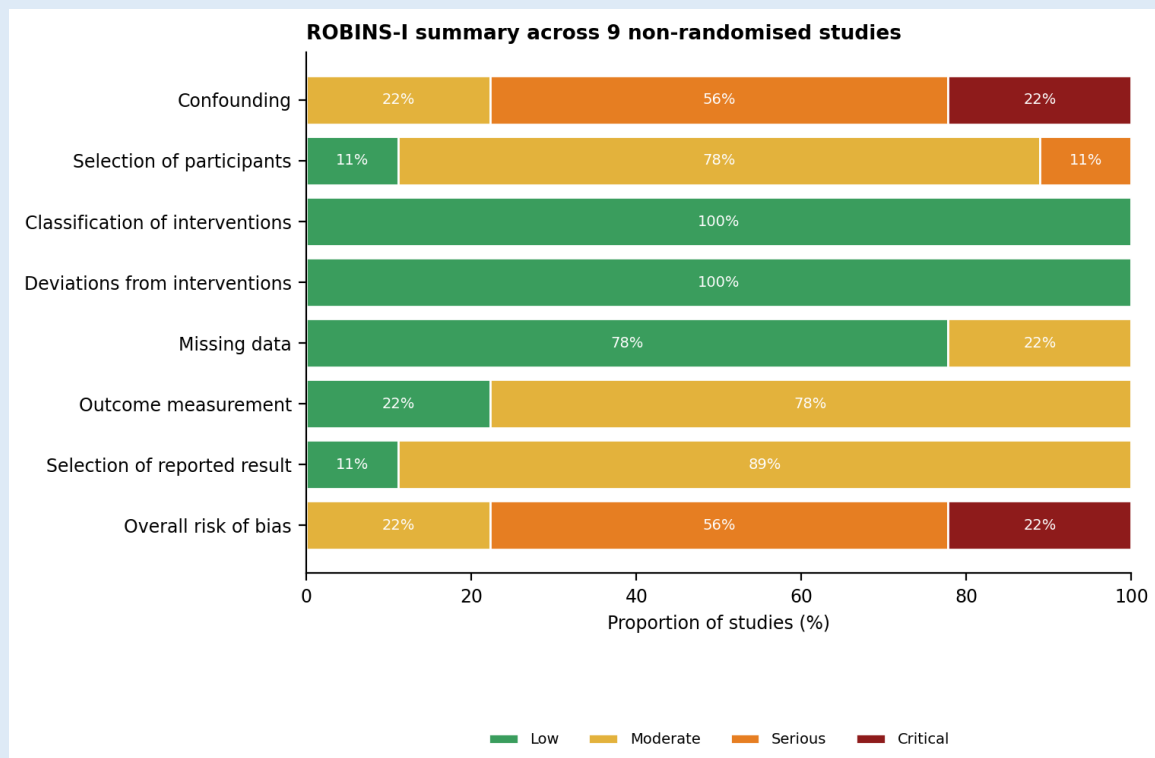


Figure 5. Summary of ROBINS-I judgements. Confounding was the dominant source of bias; two uncontrolled series were at critical risk for comparative inference.^{6,40}

Effect Measures and Data Synthesis

Dichotomous outcomes were pooled as risk ratios (RR) with 95% confidence intervals (CI) using the DerSimonian–Laird random-effects model, chosen a priori because of anticipated clinical diversity in populations, sedation and devices. A 0.5 continuity correction was applied to zero cells. For multi-arm trials, HFNC arms were combined into a single intervention group to avoid double-counting the shared control. Continuous outcomes were pooled as mean differences (MD); medians with interquartile ranges were converted to means and standard deviations with the sample-size-dependent method of Wan and colleagues, and trials reporting only an MD with 95% CI contributed through the generic inverse-variance method. For the PROSA-2 trial, which reported an adjusted odds ratio rather than event counts, and for observational studies reporting adjusted estimates, the log odds ratio (OR) and its standard error were derived from the reported CI and pooled in a separate generic inverse-variance OR analysis.^{10,56,61}

Statistical heterogeneity was quantified with Cochran's Q, I^2 and τ^2 , and 95% prediction intervals were calculated to describe the expected range of effects in a new setting. Pre-specified subgroup analyses examined sedation depth (deep sedation explicitly reported vs. topical/conscious/unspecified), procedure (EBUS-TBNA vs. non-EBUS flexible

bronchoscopy), baseline risk (high-risk populations vs. unselected) and comparator device; differences were tested with the Q-between statistic. A random-effects meta-regression tested whether control-arm risk explained heterogeneity. Sensitivity analyses comprised fixed-effect, Hartung–Knapp–Sidik–Jonkman and Paule–Mandel estimators, restriction to low-risk-of-bias trials, to nasal-cannula comparators, to explicit $\text{SpO}_2 < 90\%$ definitions, and to large (≥ 100 participants) versus small trials, together with leave-one-out and cumulative meta-analyses.^{4,62} Small-study effects were examined with contour-type funnel plots and Egger's regression test when at least ten studies contributed, and interpreted cautiously because funnel asymmetry has several causes other than publication bias. The flow–response relationship was modelled by maximum-likelihood logistic regression on arm-level data from the six-arm flow trial and compared descriptively with the four-arm deep-sedation trial. Absolute effects were derived by applying the pooled RR to the pooled control-arm risk and to a range of plausible baseline risks (10–60%), and numbers needed to treat were calculated as the reciprocal of the absolute risk reduction. Certainty of evidence was graded with the GRADE approach, with non-randomised evidence entered through ROBINS-I. All analyses were performed in Python 3.12 (NumPy, SciPy, Matplotlib) with custom code cross-checked against published estimates from the included trials; statistical significance was set at two-sided $p < 0.05$.^{11,37,40,62}

RESULTS

Characteristics of Included Studies

The 32 studies enrolled 4,572 participants: 23 RCTs (3,915 participants) and nine observational or non-randomised studies (657 participants). Publication years ranged from 2012 to 2026, with a marked acceleration after 2021; 16 studies (50%) were published in 2024–2026. Studies originated from 17 countries, most frequently China ($n = 8$), Australia/New Zealand ($n = 4$), Italy ($n = 3$) and South Korea ($n = 3$). Nineteen adult RCTs compared HFNC with a conventional low-flow strategy (nasal prongs, face mask, bite-block oxygen, nasopharyngeal tube or Venturi mask), two compared HFNC with NIV in hypoxaemic patients, one compared six HFNC flow rates, and one was conducted in children.^{8,10–13,46}

Procedures comprised diagnostic flexible bronchoscopy with or without BAL, brushing and endobronchial biopsy ($n = 12$), EBUS-TBNA ($n = 12$), bronchoscopy with TBLB in lung-transplant recipients ($n = 1$), rigid bronchoscopy under general anaesthesia ($n = 1$), mixed diagnostic/interventional series ($n = 3$) and bronchoscopy in hypoxaemic ARF ($n = 3$). Sedation ranged from topical anaesthesia alone to propofol-based deep sedation ($\text{MOAA/S} \leq 1$) and general anaesthesia with neuromuscular blockade. HFNC flows ranged from 25 to 80 L/min,

most commonly 50–60 L/min; FiO_2 was fixed (0.45–1.0) or titrated to a target SpO_2 . Two trials used a purpose-built single-prong interface to permit transnasal bronchoscopy through the contralateral nostril, and two trials deliberately matched nominal FiO_2 between arms (≈ 0.45). Desaturation thresholds varied ($\text{SpO}_2 < 90\%$ at any time, $\leq 90\%$ for > 10 s, $< 90\%$ for ≥ 30 s, $< 94\%$ in children, or a $\geq 3\%$ fall from baseline). Observational studies (Table 8) included three high-risk or hypoxaemic cohorts, two EBUS cohorts with historical or quasi-randomised controls and two uncontrolled feasibility series.^{8,9,15,38,50,52,55}

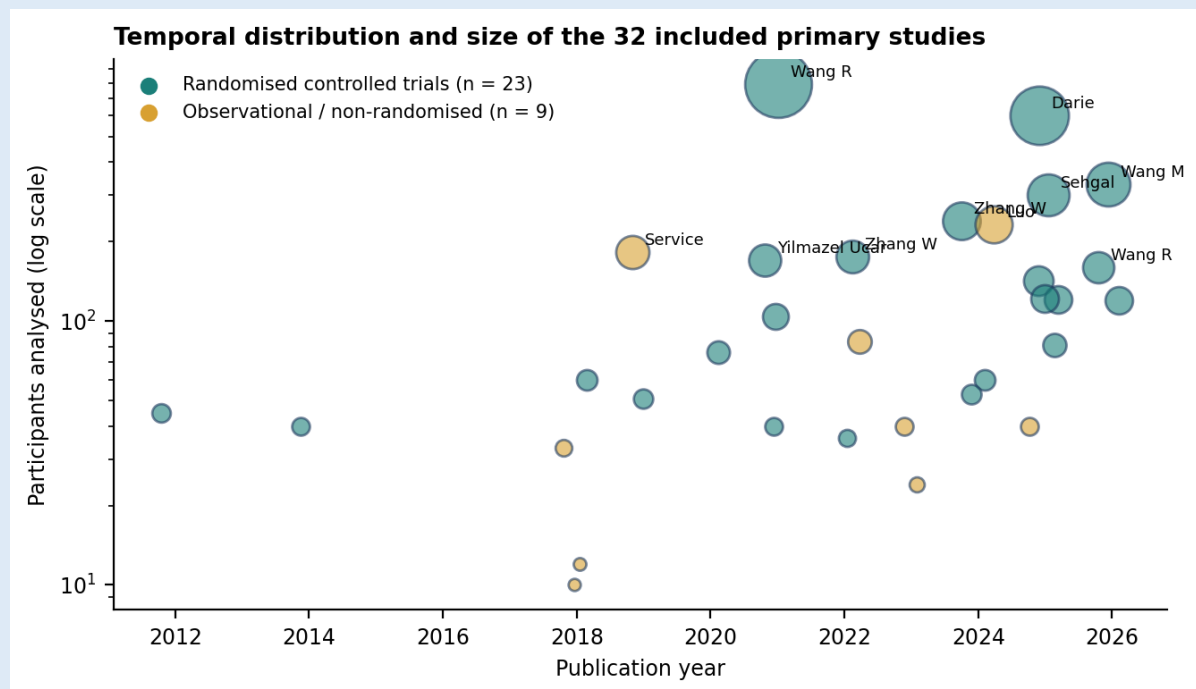


Figure 6. Temporal distribution and sample size of included studies (bubble area proportional to participants analysed; horizontal jitter applied to avoid overlap).^{8,10,36,37}

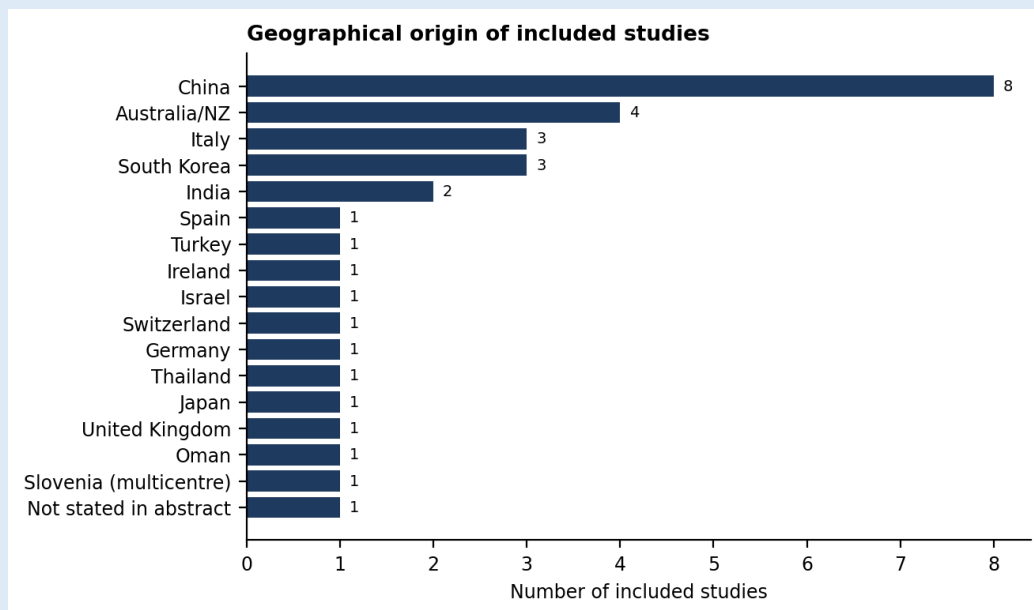


Figure 7. Geographical origin of the 32 included primary studies.⁴

Table 5. Characteristics of randomised controlled trials comparing HFNC with a conventional (low-flow) oxygen strategy in adults.

Study	Country	Design / registratio n	Population (risk profile)	N analysed (HFNC/ control)	Age (y)	Procedure / route	Sedation	HFNC settings	Comparator	Desaturation / primary endpoint
Lucangelo 2012 ⁴⁴	Italy	Single- centre RCT, 3 arms	Adults, mild respiratory dysfunction	45 (15 N40, 15 N60 / 15 VM)	NR	FB with BAL	NR	40 or 60 L/min; FiO ₂ 0.5	Venturi mask 40 L/min, FiO ₂ 0.5	End-procedure PaO ₂ , PaO ₂ /FiO ₂ , SpO ₂
Douglas 2018 ⁷	Australia	Single- centre parallel RCT	Adults undergoing EBUS	60 (30/30)	NR	EBUS; oral	Conscious (anaesthetist)	30–70 L/min	10 L/min via bite block	SpO ₂ < 90%
Ben- Menachem 2020 ⁴²	Australia	RCT; patient and bronchoscopo nist blinded	Lung-transplant recipients (high risk)	76 (37/39)	NR	FB + TBLB	Sedation	HFNO	Low-flow nasal O ₂	SpO ₂ < 94% (primary); < 90%
Yilmazel Ucar 2021 ⁴¹	Turkey	Single- centre randomised	Adults undergoing EBUS	170 (85/85)	58 ± 14	EBUS	NR	HFNC	Conventional nasal cannula	Proportion desaturating
Irfan 2021 ⁴⁵	Ireland	Single- centre parallel RCT	Adults, mediastinal disease	40 (20/20)	NR	EBUS-TBNA	Sedation	Optiflow HFNC	Nasal prongs	Fall from baseline to nadir SpO ₂
Wang R 2021 ⁸	China	Single- centre RCT (NCT02606 188)	Hospitalised; SpO ₂ ≥ 90% on air	788 (392/396)	Median 58.5	Transnasal FB, BAL, brushing, biopsy, TBLB	Topical lidocaine only	Single- prong HFNC 50 L/min; FiO ₂ to SpO ₂ > 90%	Nasal prongs ≤ 6 L/min	Any SpO ₂ < 90%
Longhini 2022 ¹⁶	Italy	Single- centre RCT (NCT04016 480)	Outpatients for BAL	36 (18/18)	NR	FB + BAL 150 mL	Topical only	60 L/min; FiO ₂ titrated	Standard therapy (O ₂ if needed)	ABG, severe desaturation, EELI

Zhang W 2022 ⁴⁷	China	Single-centre RCT (ChiCTR21 00044105)	At risk: OSA, obesity, older age, male, hypertension	176 (87/89)	NR	FB	Deep sedation	60 L/min; FiO ₂ 1.0	Tight face mask 6 L/min	Oxygen desaturation
Freund 2024 ⁴⁸	Israel	Three-arm block RCT	Adults, advanced bronchoscopy	39 (19/20)*	NR	EBUS-TBNA via bite block	Procedural sedation	HFNC	Nasal cannula (LMA arm not pooled)	Hypoxia
Kim HJ 2024 ⁴⁹	South Korea	Single-centre RCT	Adults, apnoeic rigid bronchoscopy	53 (26/27)	NR	Rigid bronchoscopy	GA + neuromuscular block	HFNO	Standard low-flow nasal O ₂	Lowest SpO ₂ ; interruptions (SpO ₂ ≤ 94%)
Qin 2025 ⁹	China	Four-centre RCT (ChiCTR21 00055038)	High risk: morbid obesity, narrow trachea, hypoxaemia/hypercapnia	142 (72/70)	NR	Nasal bronchoscopy	NR	50–60 L/min; FiO ₂ 0.45	Nasal cannula 6 L/min (matched FiO ₂)	SpO ₂ ≤ 90% > 10 s
Darje 2025 (PROSA-2) ¹⁰	Switzerland	Single-centre open-label RCT	COPD	600 (295/305)	Median 69	FB	Conscious sedation	60–80 L/min; FiO ₂ 0.6	Low flow 4–12 L/min	Cumulative hypoxaemia time; events SpO ₂ < 90%
Burton 2025 ¹⁴	Australia/NZ	RCT (ANZCTR 126230012 62695)	Unselected adults	121 (60/61)	NR	FB (n = 75) or EBUS (n = 46)	Conscious sedation	HFNO	Low-flow oxygen	Time with SpO ₂ < 90%
Sehgal 2025 (HIFLO-EBUS) ³⁶	India	RCT	Consecutive adults	300 (150/150)	46.5 ± 14	EBUS-TBNA	Conscious sedation	HFNC	Nasal cannula	SpO ₂ < 90% ≥ 30 s
Gupta 2025 ⁵⁰	India	RCT	Adults; subgroups with comorbidity	122	NR	EBUS-TBNA	NR	HFNC per protocol	Conventional nasal cannula	Fall ≥ 3% from baseline
Yue 2025 ⁵¹	China	RCT (ChiCTR24 00085320)	Adults	81 (41/40)	NR	EBUS-TBNA	Anaesthesia-led sedation	45 L/min	Nasopharyngeal tube 6 L/min	Hypoxia incidence
Rozman 2026 ¹⁵	Slovenia-led (4 centres)	Multicentre RCT	Adults	120 (57/63)	NR	Oral EBUS-TBNA	Moderate-to-deep, standardised	60 L/min; FiO ₂ 0.45	Nasal cannula 6 L/min (FiO ₂ ≈ 0.45)	Proportion without SpO ₂ < 90% > 10 s

Wang M 2026 ³⁷	China	Four-arm RCT (ChiCTR24 00083597)	ASA I–II	330 (246 HFNC [83/83/80] / 84)	NR	Diagnostic FB	Deep sedation (MOAA/S ≤ 1)	25, 45 or 65 L/min	Nasal cannula 5 L/min	SpO ₂ < 90% > 10 s; nadir SpO ₂
Wang R 2026 ³⁸	China	Two-centre open-label RCT (NCT05759 832)	Acute respiratory failure	160 (80/80)	NR	Nasal FB	NR	Single-prong HFNO	Standard oxygen therapy	Escalation of respiratory support ≤ 24 h

**Three-arm trial (20 per arm); one HFNC patient not analysed; laryngeal-mask arm excluded from pooling. ABG, arterial blood gas; ASA, American Society of Anesthesiologists physical status; EELI, end-expiratory lung impedance; FB, flexible bronchoscopy; GA, general anaesthesia; HFNO, high-flow nasal oxygen; LMA, laryngeal mask airway; MOAA/S, Modified Observer's Assessment of Alertness/Sedation; NR, not reported in the accessible report; OSA, obstructive sleep apnoea; VM, Venturi mask.*

Table 6. Characteristics of other randomised trials (paediatric, HFNC versus NIV and flow-comparison designs).

Study	Country	Design	Population	N	Intervention	Comparator	Principal oxygenation finding
Sharluyan 2021 ⁴⁶	Spain	Single-centre open-label RCT	Children 1 month–16 years, elective FB	104 (51/53)	HFNC	Standard low-flow nasal prongs	Fewer desaturations (SpO ₂ < 94%); ARR 0.27 (95% CI 0.08–0.45); NNT 3.75; greatest benefit with BAL
Simon 2014 ¹²	Germany	ICU RCT (NCT01870765)	Acute hypoxaemic respiratory failure	40	HFNC	NIV	Oxygenation higher with NIV before, during and after FB; two HFNC patients could not proceed
Saksitthichok 2019 ¹³	Thailand	Prospective RCT	PaO ₂ < 70 mmHg on room air	51 (26/25)	HFNC	NIV	Lowest SpO ₂ similar; SpO ₂ < 90% 34.6% vs 12.0% (p = 0.057); NIV superior when PaO ₂ < 60 mmHg
Zhang W 2024 ¹¹	China	Six-arm RCT (NCT05298319)	Adults, propofol sedation	240 (40 per arm)	HFNC 10–60 L/min, FiO ₂ 1.0	Lower HFNC flows	Desaturation 42.5% → 0% from 10 to 60 L/min; ED ₉₅ 43.2 L/min (95% CI 36.4–56.0)

ARR, absolute risk reduction; ED₉₅, effective flow preventing desaturation in 95% of patients; NNT, number needed to treat.

Table 7. Characteristics of observational and non-randomised comparative studies.

Study	Country	Design	Population / procedure	N (HFNC/control)	HFNC settings	Comparator	Principal oxygenation finding
Takakuwa 2018 ⁵²	Japan	Prospective pilot + historical control	EBUS-TBNA, midazolam sedation	12 HFNC + historical controls	FiO ₂ 0.30, titrated to SpO ₂ > 90%	Conventional nasal cannula (historical)	Mean lowest SpO ₂ 93% vs 88% (p = 0.005)
Kim EJ 2018 ⁵³	South Korea	Retrospective cohort	ARF (P/F ≤ 300), BAL	33 procedures	Flow 49 ± 7 L/min; FiO ₂ 0.74 during BAL	"Without HFNC" group (milder ARF)	SpO ₂ 94.8 → 94.6 → 95.2% before/during/after; no intubation ≤ 24 h
Chung 2018 ⁵⁴	South Korea	Retrospective case series	Hypoxaemic diagnostic/interventional FB	10	HFNC	None	Mean lowest intraprocedural SpO ₂ 95%; all procedures tolerated
Service 2019 ⁵⁵	United Kingdom	Prospective feasibility cohort	Outpatient FB/EBUS, anaesthetist-led remifentanyl ± propofol	182	10–70 L/min	None	10 patients transiently < 89%; all procedures completed
Nilushi 2022 ⁵⁶	Australia	Prospective sequential allocation	Outpatient FB and EBUS, conscious sedation	84 (42/42)	HFNO	LFNO	Adjusted OR for hypoxaemia with LFNO 13.8 (3.55–70.7)
Arias-Sánchez 2023 ⁵⁷	NR	Prospective observational	Pneumonia, oral FB for bronchial aspirate	40 (20/20)	60 L/min; FiO ₂ 0.40	Standard O ₂ , FiO ₂ 0.40	Nadir SpO ₂ 94% vs 90%; ΔSpO ₂ 2% vs 4.5%
Ravi 2023 ⁵⁸	Oman	Quasi-randomised pilot	Oncological EBUS-TBNA, moderate sedation	24 (10/14)	HFNO	Supraglottic airway device	Lowest SpO ₂ 93.5 ± 4.5% vs 90 ± 3%
Luo 2024 ⁵⁹	China	Retrospective cohort 2018–2023	Pre-existing hypoxaemia, FB	232 (78/154)	HFNC	Nasal cannula	Lowest SpO ₂ < 90%: 3.8% vs 17.5%; adverse events 7.7% vs 20.1%
de Vico 2025 ⁶⁰	Italy	Prospective observational	ASA III, EBUS-TBNA, midazolam + propofol	40 (20/20)	HFNC	Standard low-flow	Lowest SpO ₂ 91.4 ± 5.9 vs 83.2 ± 15.6%; SpO ₂ drop 3.8 vs 12.3 points

LFNO, low-flow nasal oxygen; NR, not reported in the accessible abstract; P/F, PaO₂/FiO₂ ratio.

Table 8. Study-level oxygenation, procedural and safety findings of randomised trials of HFNC versus conventional oxygen.

Study	Desaturation HFNC vs control	Nadir SpO ₂ (HFNC vs control)	Procedural outcomes	Gas exchange / CO ₂	Comfort / safety	Direction
Lucangelo 2012 ⁴⁴	NR	End-procedure SpO ₂ highest with N60	—	Higher PaO ₂ and PaO ₂ /FiO ₂ with N60; N40 ≈ Venturi 40	Airway pressure 3.6 cmH ₂ O at 60 L/min (volunteers)	Favours HFNC 60
Douglas 2018 ⁷	4/30 vs 10/30 (ITT p = 0.07; PP p = 0.047)	Median 97.5 vs 92 (p < 0.001)	No difference in hypoxic episodes	EtCO ₂ similar	No difference	Favours HFNC
Ben-Menachem 2020 ⁴²	< 90%: 16.2% vs 69.2%; < 94%: 43.2% vs 89.7%	NR	0 vs 11 interruptions (9 patients)	—	Anaesthetist satisfaction higher	Favours HFNC
Yilmazel Ucar 2021 ⁴¹	5/85 vs 26/85 (p < 0.001)	End-procedure SpO ₂ higher	—	Heart rate 96 vs 101 (NS)	Discomfort 5 vs 18 (p = 0.006)	Favours HFNC
Irfan 2021 ⁴⁵	Drop 7.7 points smaller (4.91–10.49)	MD +9.2 (6.44–11.96)	—	No difference in venous CO ₂	VAS and willingness to repeat similar	Favours HFNC
Wang R 2021 ⁸	49/392 (12.5%) vs 114/396 (28.8%)	94.1 ± 3.2 vs 90.5 ± 3.8	Discontinuation 9.9% vs 25.8%; duration 685 vs 800 s	Lower RR and HR during FB	Pneumothorax 2.6% vs 5.8%; agitation 11.0% vs 19.2%	Favours HFNC
Longhini 2022 ¹⁶	11% vs 56%	Nadir ≈ 95% vs 89%	—	PaO ₂ at end 11.1 vs 9.1 kPa; EELI preserved	Less diaphragm activation	Favours HFNC
Zhang W 2022 ⁴⁷	4/87 (4.6%) vs 26/89 (29.2%)	NR	Jaw thrust 5.7% vs 48.3%; bag-mask 0 vs 9.0%	—	—	Favours HFNC
Freund 2024 ⁴⁸	26% vs 90%	NR	Interventions 52.6% vs 90%	—	Fewer complications (multivariable)	Favours HFNC
Kim HJ 2024 ⁴⁹	NR	Median 99 vs 98 (p = 0.059)	Interruptions 3.8% vs 29.6%	PaO ₂ decline 4.6 vs 10.5 mmHg/min; PaCO ₂ rise 1.6 vs 2.0 mmHg/min	—	Favours HFNC
Qin 2025 ⁹	34.7% vs 61.4% (p = 0.016)	Median 94 vs 87.5	Interruption 26.4% vs 58.6%; escalation 30.6% vs 57.1%	Peak PtcCO ₂ 64.6 vs 68.3 mmHg	Adverse events similar	Favours HFNC

Darje 2025 ¹⁰	OR for hypoxaemia with low flow 5.1 (3.2–8.2)	NR	Hypoxaemia events median 3 vs 6	Hypoxaemia time 1.8% vs 3.8% of monitoring	Comfort not different	Favours HFNC
Burton 2025 ¹⁴	No difference	No difference	Fewer O ₂ titrations (NS)	Lower respiratory rate in EBUS	Clinician satisfaction higher	Neutral
Sehgal 2025 ³⁶	30/150 (20%) vs 64/150 (42.7%)	Median 93 vs 91	Fewer desaturation events (MD 0.55)	—	Comfort better (VAS +7.1 mm); complications similar	Favours HFNC
Gupta 2025 ⁵⁰	No overall difference	NR	—	tcCO ₂ rise similar	Benefit in comorbid and SpO ₂ < 97% subgroups	Neutral overall
Yue 2025 ⁵¹	2/41 (4.9%) vs 10/40 (25.0%)	NR	Fewer jaw lifts and mask ventilation	Higher PaO ₂ , lower PaCO ₂	Adverse events similar	Favours HFNC
Rozman 2026 ¹⁵	25/57 (44%) vs 36/63 (57%) (p = 0.20)	Higher with HFNC (p = 0.01)	Persistent desaturation 7% vs 21%	—	No advanced airway needed	Partly favours HFNC
Wang M 2026 ³⁷	16.9/12.0/5.0% vs 57.1%	Higher in all HFNC arms	No LMA or intubation needed	Less CO ₂ retention	> 97% willing to repeat	Favours HFNC
Wang R 2026 ³⁸	—	—	Escalation 15.0% vs 33.8%; intubation 7.5% vs 20.0%	Smaller EELI and tidal impedance loss	—	Favours HFNC

HR, heart rate; ITT, intention-to-treat; NS, not significant; PP, per-protocol; PtcCO₂/tcCO₂, transcutaneous CO₂; RR, respiratory rate; VAS, visual analogue scale.

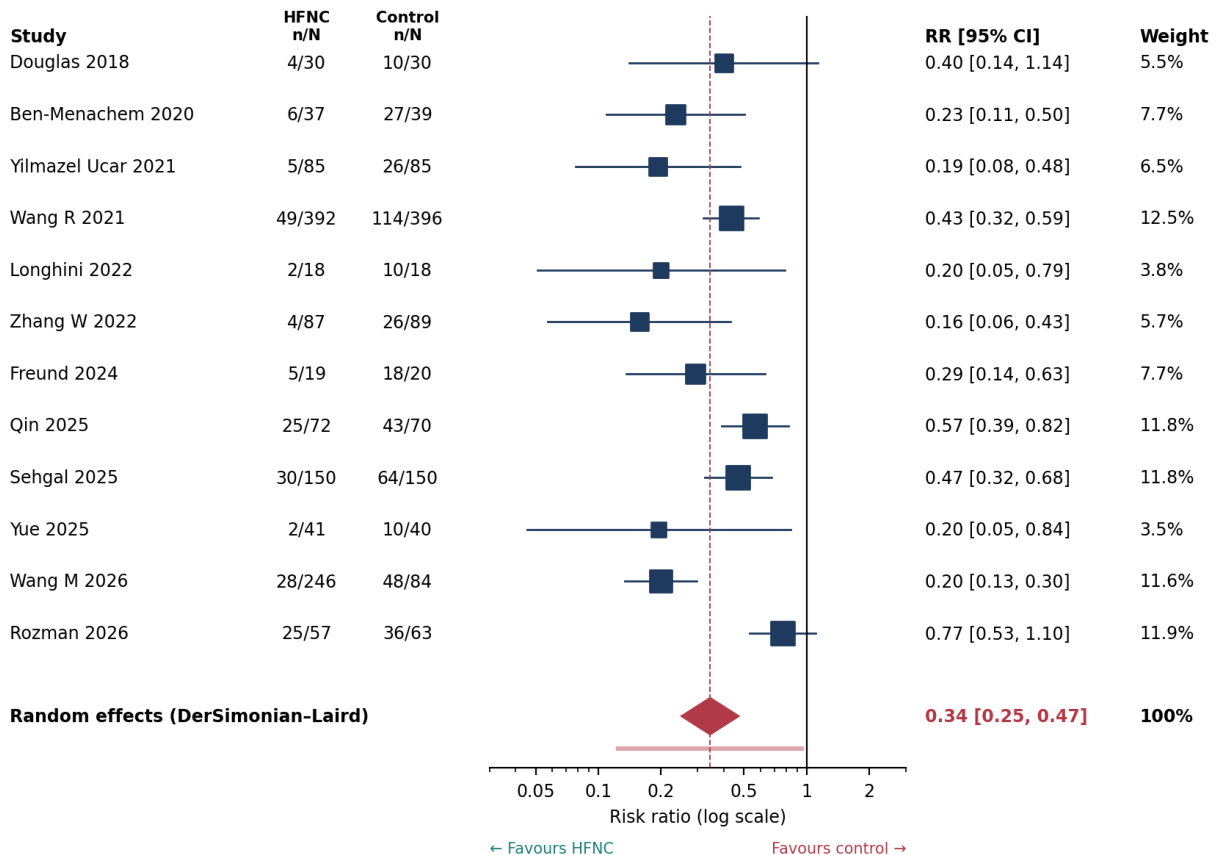
Risk of Bias in Included Studies

Among the 23 RCTs, seven (30%) were judged at low overall risk of bias, 15 (65%) raised some concerns and one (4%) was at high risk. The randomisation process was generally adequate, whereas the dominant concerns arose from deviations from intended interventions (open-label delivery with discretionary FiO₂ titration and rescue manoeuvres) and from outcome measurement when desaturation was recorded manually or defined idiosyncratically. Among the nine non-randomised studies, two were at moderate, five at serious and two at critical risk of bias, predominantly owing to confounding by indication and the use of historical or no controls.^{5,6,8,50}

Primary Outcome: Incidence of Intraprocedural Desaturation

Twelve adult RCTs (2,318 participants; 1,234 HFNC and 1,084 control) contributed event data. Desaturation occurred in 185 of 1,234 HFNC patients (15.0%) and 432 of 1,084 control patients (39.9%). HFNC reduced the risk of desaturation by approximately two-thirds (pooled RR 0.34, 95% CI 0.25–0.47; $Z = 6.67$, $p < 0.001$). Heterogeneity was substantial ($\tau^2 = 0.181$; $I^2 = 71.7\%$; $Q = 38.86$, $df = 11$, $p < 0.001$), but all point estimates favoured HFNC and the 95% prediction interval (0.12–0.95) excluded the null, indicating that a benefit is expected in a new comparable setting (Figure 9). The largest effects were observed under deep sedation with high flows (Wang M 2026, RR 0.20; Zhang W 2022, RR 0.16), and the smallest in the FiO₂-matched EBUS trial (Rozman 2026, RR 0.77, 95% CI 0.53–1.10) and the high-risk nasal-bronchoscopy trial (Qin 2025, RR 0.57).^{7–9,15,16,36,37,41,42,47,48,51}

Intraprocedural oxygen desaturation (SpO₂ < 90%): HFNC versus conventional oxygen — adult RCTs



Heterogeneity: $\tau^2 = 0.181$; $Q = 38.86$, $df = 11$ ($p < 0.001$); $I^2 = 71.7\%$. Overall effect: $Z = 6.67$ ($p < 0.001$); 95% prediction interval 0.12–0.95

Figure 8. Forest plot of the primary outcome. Random-effects (DerSimonian–Laird) pooled risk ratio for intraprocedural desaturation with HFNC versus conventional oxygen in 12 adult RCTs. Square size is proportional to study weight; the diamond shows the pooled estimate and the pale bar beneath it the 95% prediction interval.^{7–9,15,16,36,37,41,42,47,48,51}

Control-arm desaturation ranged from 25% to 90%, whereas HFNC-arm rates ranged from 4.6% to 44%. The L'Abbé plot shows every trial below the line of equality, with most clustered around the line representing the pooled RR, graphically confirming consistency of direction despite statistical heterogeneity in magnitude.^{15,47,48}

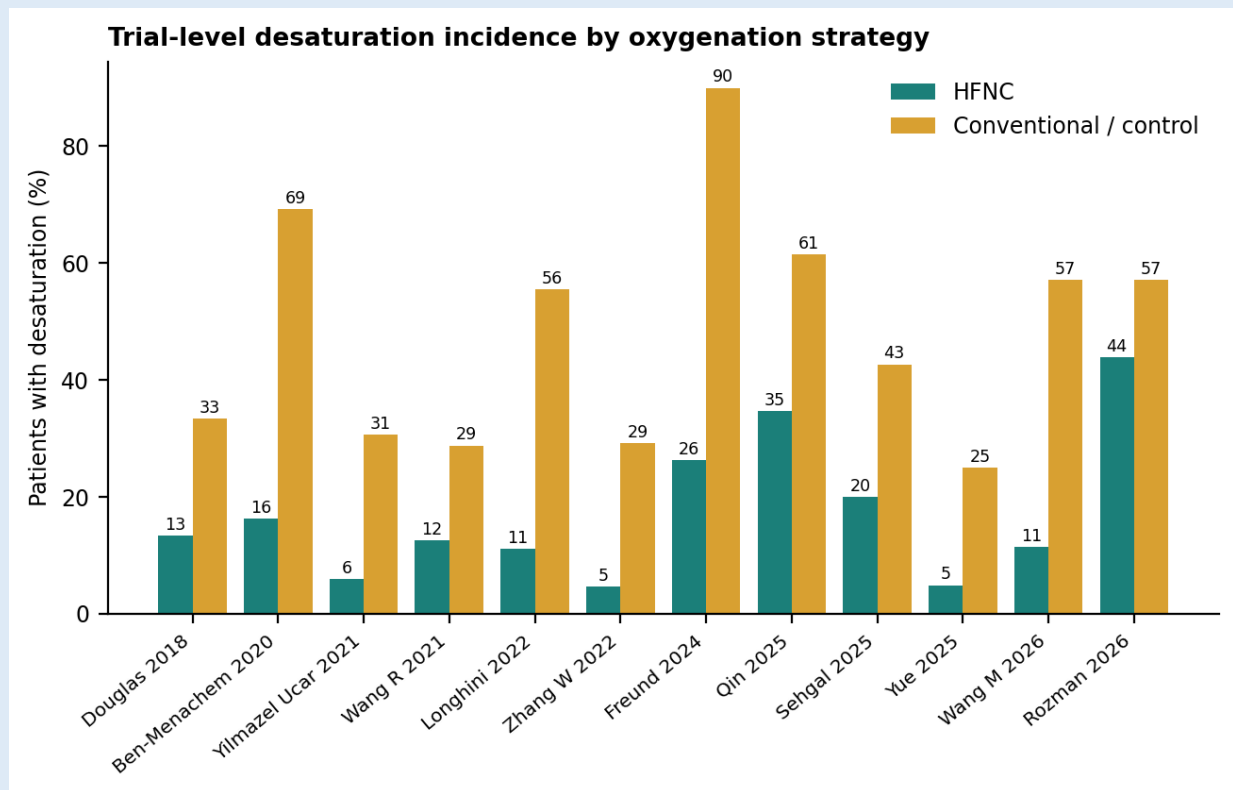


Figure 9. Trial-level incidence of desaturation (%) in HFNC and control arms of the 12 RCTs contributing to the primary analysis.^{8,9,36}

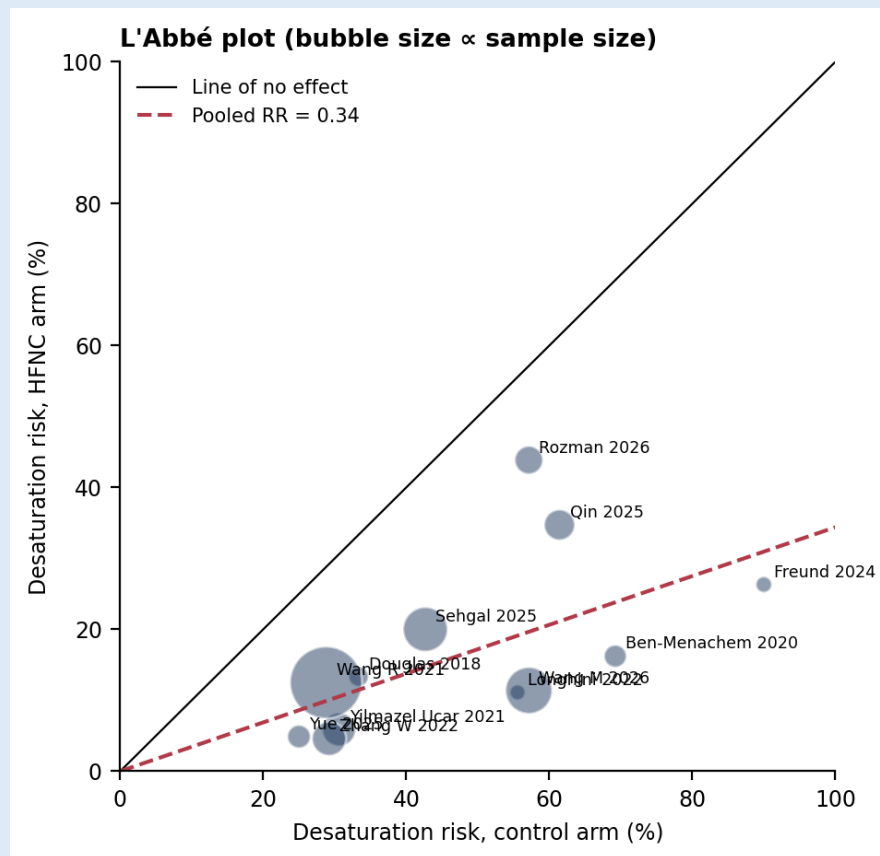


Figure 10. L'Abbé plot of desaturation risk in HFNC versus control arms (bubble area proportional to sample size). The solid line indicates no effect and the dashed line the pooled risk ratio.^{8,37}

Odds-ratio analysis including PROSA-2 and observational studies

Because the PROSA-2 trial in 600 patients with COPD reported an odds ratio (low flow vs. high flow OR 5.1, 95% CI 3.2–8.2) rather than event counts, a complementary generic inverse-variance OR analysis was performed. Across 13 RCTs the pooled OR was 0.20 (95% CI 0.14–0.30; $I^2 = 64.7\%$), and in two comparative observational studies it was 0.13 (0.05–0.33; $I^2 = 0\%$), with no difference between designs ($Q = 0.81$, $p = 0.37$). Combining all 15 studies yielded an OR of 0.20 (0.14–0.28; $I^2 = 61.7\%$; prediction interval 0.06–0.61).^{10,56,59}

Desaturation expressed as odds ratio, including PROSA-2 (reported OR) and observational comparative studies

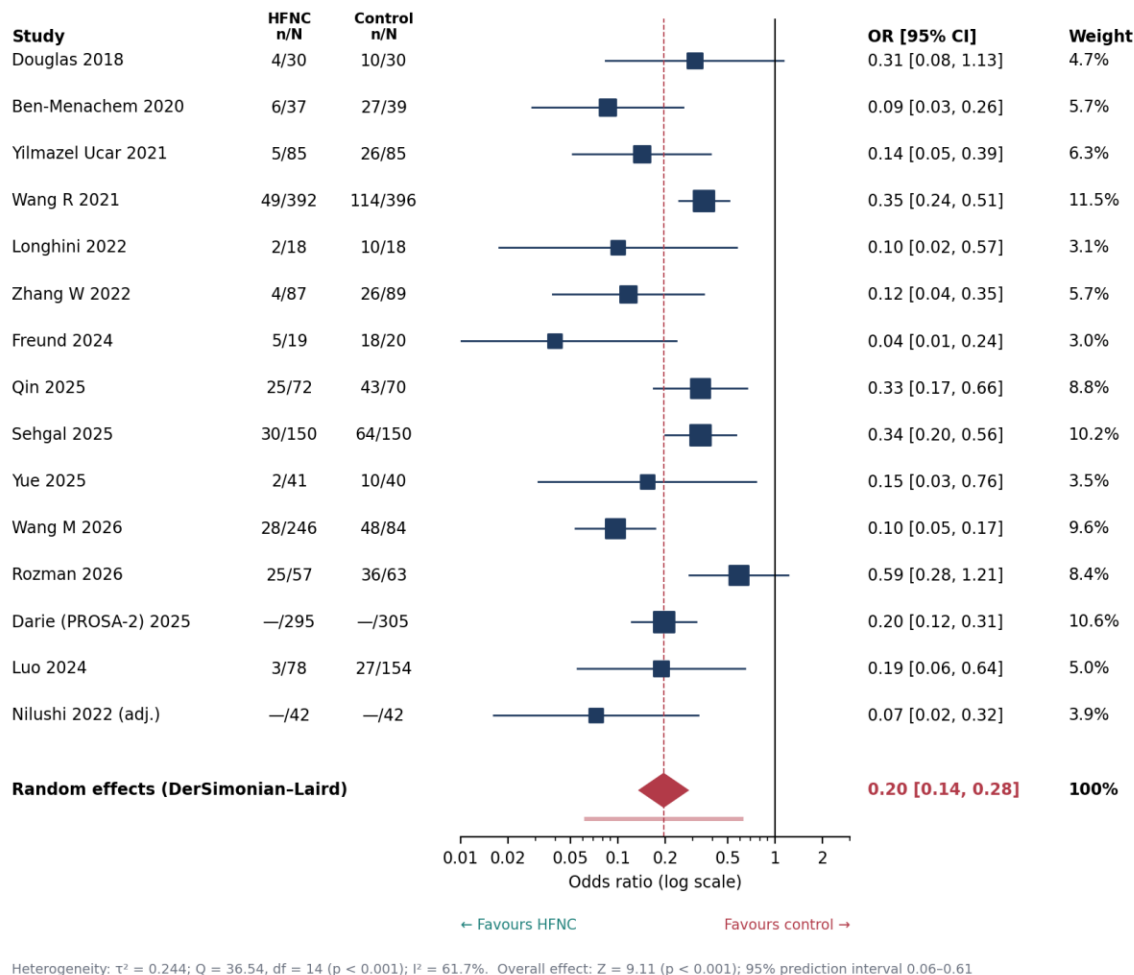


Figure 11. Desaturation expressed as odds ratios, adding the PROSA-2 trial (reported OR, inverted to HFNC vs. low flow) and two observational comparative studies (Luo 2024, crude; Nilushi 2022, adjusted) to the 12 RCTs.^{10,56,59}

Exploration of Heterogeneity

Pre-specified subgroup analyses did not identify a statistically significant effect modifier. The benefit was similar with deep sedation explicitly reported (RR 0.30, 0.10–0.89; $k = 3$) and with topical, conscious or unspecified sedation (RR 0.39, 0.31–0.50; $k = 9$; p for interaction = 0.64), in

EBUS-TBNA (RR 0.40, 0.26–0.63) and non-EBUS flexible bronchoscopy (RR 0.30, 0.19–0.47; $p = 0.36$), and in high-risk (RR 0.30, 0.13–0.68) and unselected populations (RR 0.35, 0.24–0.51; $p = 0.75$). Point estimates were larger against face-mask and nasopharyngeal comparators than against nasal prongs, but these subgroups contained single trials ($p = 0.38$). Notably, heterogeneity within the non-deep sedation stratum was low ($I^2 = 28\%$), whereas it was very high within the deep-sedation stratum ($I^2 = 93\%$), where the FiO₂-matched Rozman trial contrasted with two high-flow, high-FiO₂ trials.^{9,15,37,42,47}

Table 9. Subgroup analyses of the primary outcome (random effects).

Subgroup	k	RR (95% CI)	p	I ² (%)	τ ²
Sedation depth — test for subgroup differences: Q = 0.22, df = 1, p = 0.643					
Topical / conscious / not specified	9	0.39 (0.31–0.50)	< 0.001	27.6	0.032
Deep sedation explicitly reported	3	0.30 (0.10–0.89)	0.029	92.7	0.799
Procedure — test for subgroup differences: Q = 0.85, df = 1, p = 0.357					
EBUS-TBNA	6	0.40 (0.26–0.63)	< 0.001	62.6	0.166
Flexible bronchoscopy (non-EBUS)	6	0.30 (0.19–0.47)	< 0.001	75.5	0.199
Baseline risk of hypoxaemia — test for subgroup differences: Q = 0.10, df = 1, p = 0.754					
Unselected / standard risk	9	0.35 (0.24–0.51)	< 0.001	73.7	0.197
High-risk populations	3	0.30 (0.13–0.68)	0.004	76.1	0.386
Comparator device — test for subgroup differences: Q = 3.07, df = 3, p = 0.381					
Bite-block O ₂	1	0.40 (0.14–1.14)	0.085	0.0	0.000
Nasal cannula	9	0.37 (0.26–0.52)	< 0.001	76.7	0.183
Face mask	1	0.16 (0.06–0.43)	< 0.001	0.0	0.000
Nasopharyngeal tube	1	0.20 (0.05–0.84)	0.028	0.0	0.000

k, number of trials; *RR*, risk ratio; τ^2 , between-study variance.

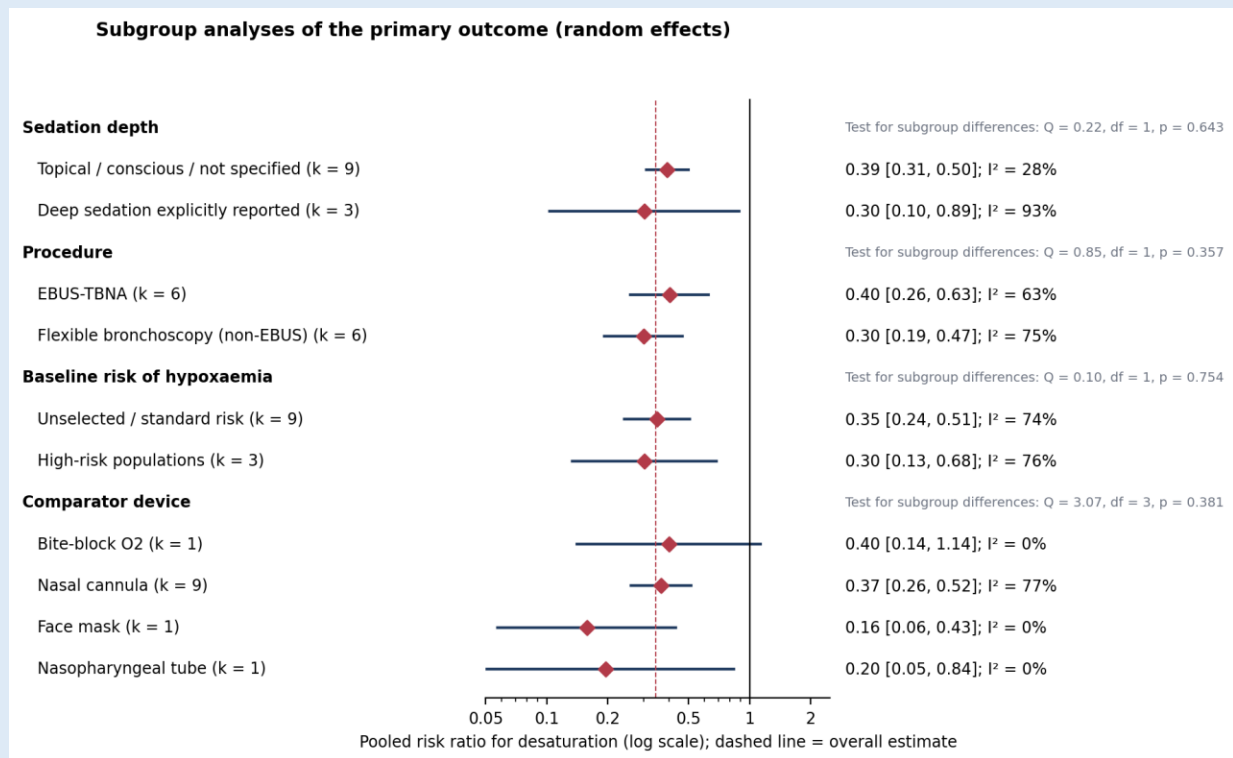


Figure 12. Subgroup analyses of the primary outcome by sedation depth, procedure, baseline risk and comparator device. The dashed line marks the overall pooled RR.⁵

In random-effects meta-regression, control-arm desaturation risk did not explain heterogeneity (slope 0.26 per unit risk on the log-RR scale, $p = 0.77$), indicating a roughly constant relative effect across baseline risk and therefore larger absolute benefit where baseline risk is higher.⁶²

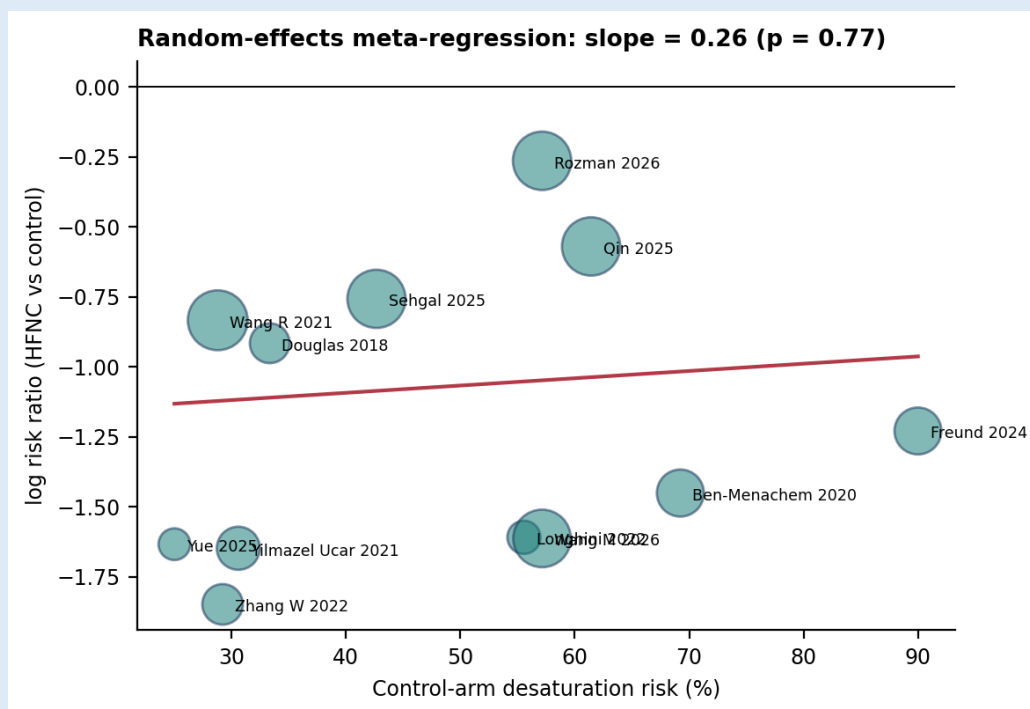


Figure 13. Bubble plot of random-effects meta-regression of the log risk ratio on control-arm desaturation risk (bubble size proportional to inverse-variance weight).⁶²

Sensitivity Analyses

The primary estimate was robust. Alternative estimators produced near-identical results (fixed effect RR 0.41, 0.35–0.47; Hartung–Knapp 0.34, 0.25–0.48; Paule–Mandel 0.35, 0.26–0.47). Restricting to the two low-risk-of-bias trials yielded RR 0.23 (0.12–0.44; $I^2 = 0\%$). Leave-one-out estimates ranged from 0.32 (omitting Qin 2025) to 0.39 (omitting Wang M 2026) and remained significant in every iteration. Omitting both Wang M 2026 and Rozman 2026 reduced I^2 from 72% to 38% while leaving the effect unchanged (RR 0.36, 0.28–0.47), identifying these two trials—one with the highest flow and deep sedation, the other with matched nominal FiO_2 —as the principal sources of heterogeneity. Cumulative meta-analysis showed that the pooled estimate became statistically significant with the second trial in 2020 and has remained stable between 0.28 and 0.39 since (Figure 16).^{9,15,16,37,42}

Table 10. Sensitivity analyses for the primary outcome.

Analysis	k	Participants	RR (95% CI)	I^2 (%)
----------	---	--------------	-------------	-----------

Primary analysis (DerSimonian–Laird)	12	2,318	0.34 (0.25–0.47)	71.7
Fixed-effect (inverse variance)	12	2,318	0.41 (0.35–0.47)	—
Hartung–Knapp–Sidik–Jonkman	12	2,318	0.34 (0.25–0.48)	—
Paule–Mandel τ^2 estimator	12	2,318	0.35 (0.26–0.47)	—
Low overall risk of bias only	2	112	0.23 (0.12–0.44)	0.0
Nasal-cannula comparators only	9	2,001	0.37 (0.26–0.52)	76.7
Explicit SpO ₂ < 90% definition only	10	2,109	0.36 (0.26–0.51)	74.5
Trials with ≥ 100 participants	7	2,026	0.38 (0.26–0.56)	82.1
Trials with < 100 participants	5	292	0.27 (0.17–0.41)	0.0
Excluding Wang M 2026 and Rozman 2026	10	1,868	0.36 (0.28–0.47)	38.2
Odds ratio, 13 RCTs incl. PROSA-2	13	2,918	OR 0.20 (0.14–0.30)	64.7
Odds ratio, all RCTs + observational	15	3,234	OR 0.20 (0.14–0.28)	61.7

Small trials showed somewhat larger effects than large trials, consistent with small-study effects (see Section 3.7), but the direction and significance of the effect were preserved in every stratum.

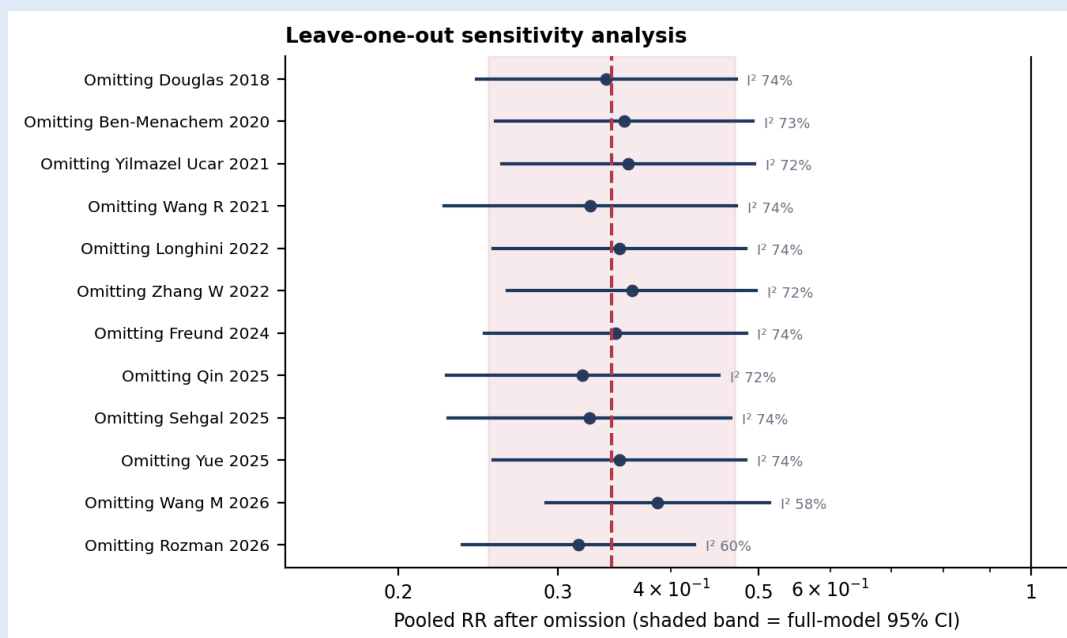


Figure 14. Leave-one-out sensitivity analysis. Each row shows the pooled RR after omitting the named trial; the shaded band represents the 95% CI of the full model.^{9,15,37}

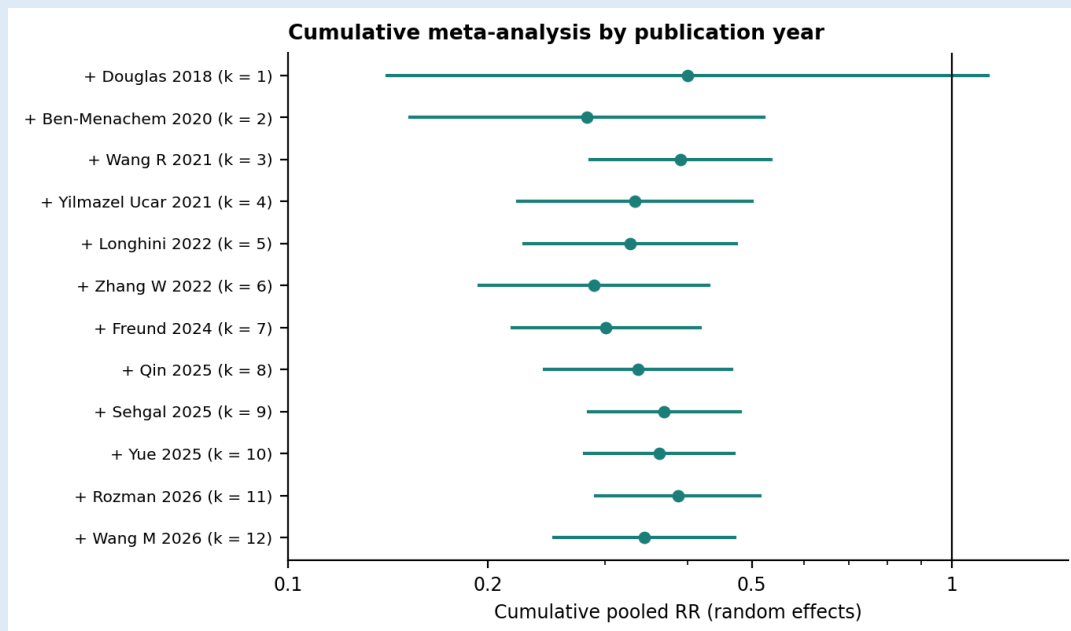


Figure 15. Cumulative random-effects meta-analysis by year of publication, showing early and sustained stabilisation of the pooled RR.^{7,42}

Small-Study Effects and Reporting Bias

The funnel plot for the primary outcome showed mild asymmetry, with smaller trials tending to report larger relative benefits. Egger's regression intercept was -2.05 (SE 1.05 ; $p = 0.080$), which does not reach conventional significance but warrants caution. Because the two largest trials (Wang R 2021, $n = 788$; Sehgal 2025, $n = 300$) and the pooled estimate from trials with ≥ 100 participants (RR 0.38) closely matched the overall result, small-study effects are unlikely to explain the benefit, although they may modestly inflate its magnitude.^{8,36,62}

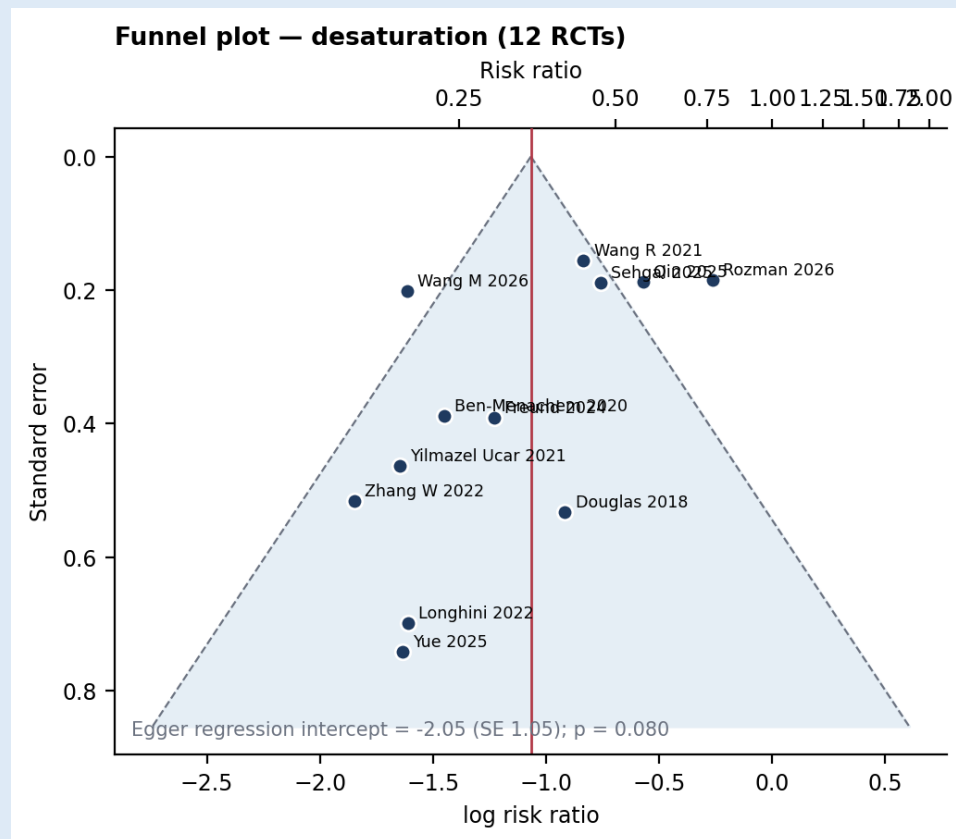


Figure 16. Funnel plot of the log risk ratio against its standard error for the 12 RCTs of the primary outcome, with pseudo-95% confidence limits and Egger's test.⁶²

Secondary Outcome: Nadir SpO₂

Five RCTs (1,083 participants) contributed nadir SpO₂ data. HFNC raised the lowest intraprocedural SpO₂ by 4.95 percentage points (95% CI 2.89–7.00; $p < 0.001$), with substantial heterogeneity ($I^2 = 83.6\%$; prediction interval –2.39 to 12.29). Adding the prospective observational study of ASA III patients yielded a comparable estimate (MD 5.13, 3.14–7.12; $I^2 = 80.6\%$). The smallest difference occurred during apnoeic rigid bronchoscopy under general anaesthesia (MD 1.67, –0.20 to 3.54), where both groups remained well oxygenated, and the largest during EBUS-TBNA (Irfan 2021, MD 9.2; de Vico 2025, MD 8.2). Control arms frequently approached or crossed the 90% threshold, whereas HFNC arms remained above 91% in all studies. Egger's test for this outcome (six studies, exploratory) was not significant (intercept 1.65; $p = 0.24$).^{7–9,45,49,60,61}

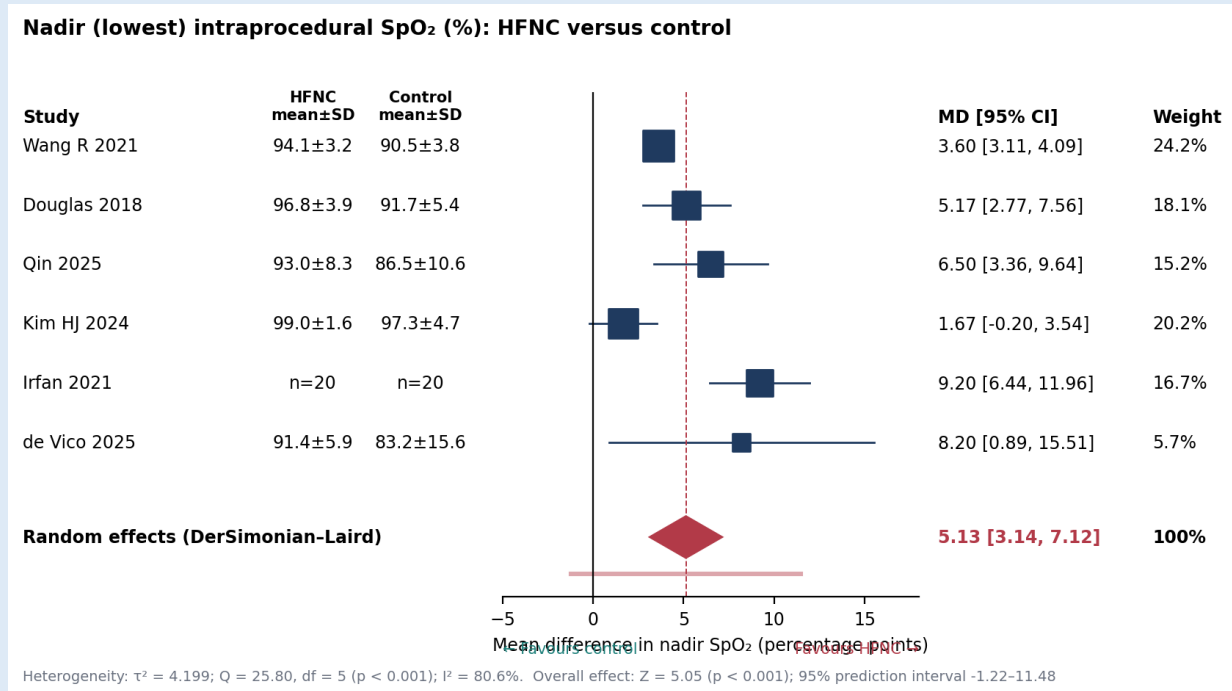


Figure 17. Forest plot of the mean difference in nadir SpO₂ (percentage points). Medians and interquartile ranges were converted to means and SDs (Douglas 2018, Qin 2025, Kim HJ 2024); Irfan 2021 contributed its reported MD and 95% CI. de Vico 2025 is observational.^{45,60,61}

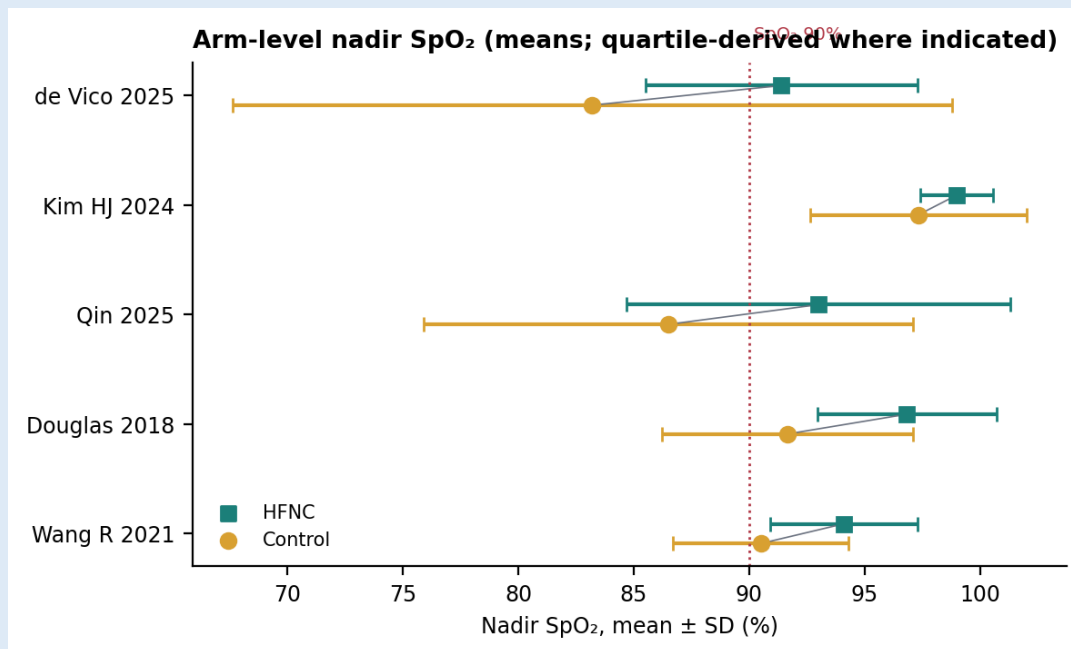


Figure 18. Arm-level nadir SpO₂ (mean ± SD) in HFNC and control groups; the dotted line marks SpO₂ 90%.^{8,9,60}

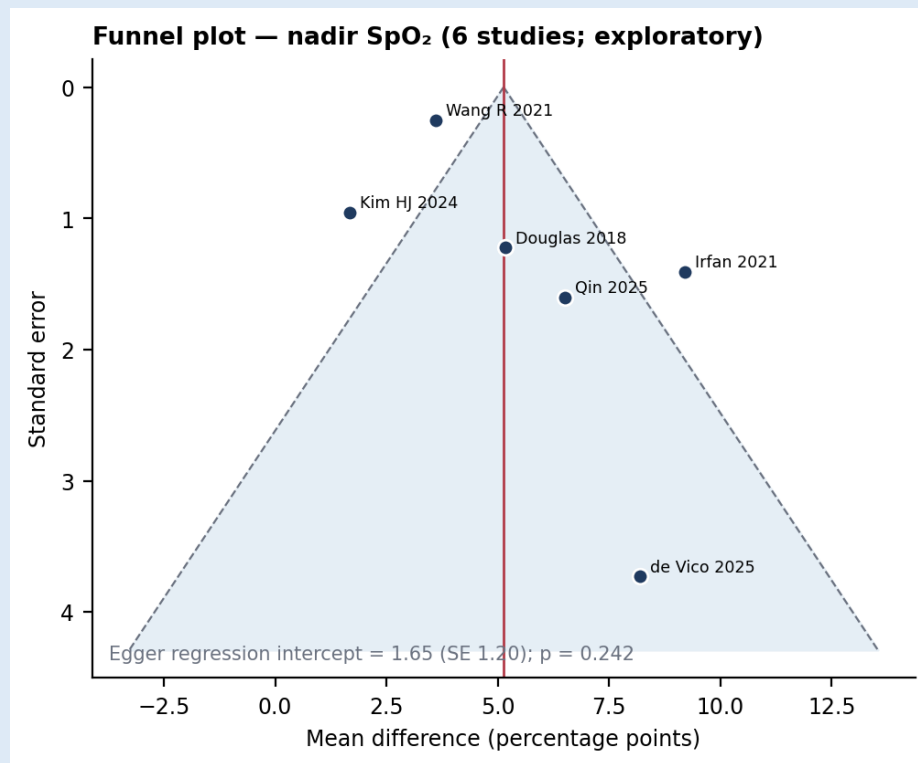


Figure 19. Exploratory funnel plot for nadir SpO₂ (six studies).⁶²

Procedure Interruption

Four RCTs (1,059 participants) reported interruption or discontinuation of bronchoscopy due to hypoxaemia: 59 of 527 (11.2%) with HFNC versus 160 of 532 (30.1%) with control (RR 0.39, 95% CI 0.28–0.54; $I^2 = 12.5\%$; prediction interval 0.16–0.94), equivalent to 183 fewer interruptions per 1,000 procedures. Consistently, bronchoscopy duration was shorter with HFNC in the largest trial (median 685 vs. 800 s).^{8,9,42,49}

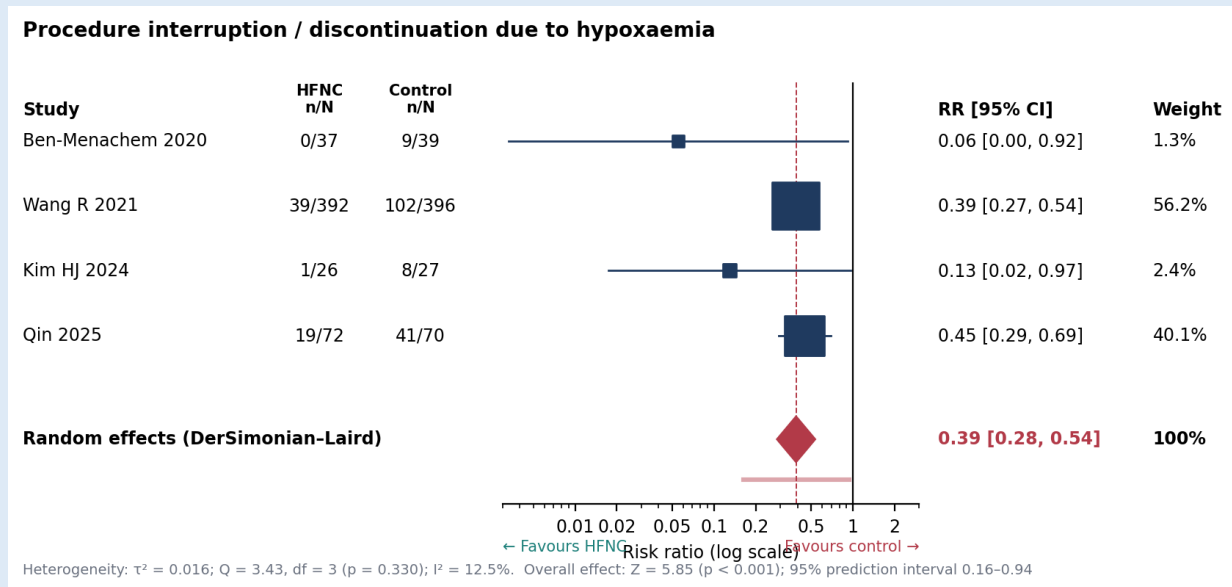


Figure 20. Forest plot of procedure interruption or discontinuation because of hypoxaemia.^{8,9,42,49}

Airway Manoeuvres and Escalation of Respiratory Support

Four RCTs (517 participants) reported the need for airway manoeuvres or escalation: 49 of 258 (19.0%) versus 128 of 259 (49.4%) (RR 0.40, 0.24–0.67; $I^2 = 72.1\%$). The largest effect concerned jaw-thrust manoeuvres under deep sedation (5.7% vs. 48.3%), and in ARF the single-prong HFNO interface reduced escalation of respiratory support within 24 h from 33.8% to 15.0%. Heterogeneity reflects differing definitions, and the prediction interval (0.04–3.67) was wide.^{9,38,47,48}

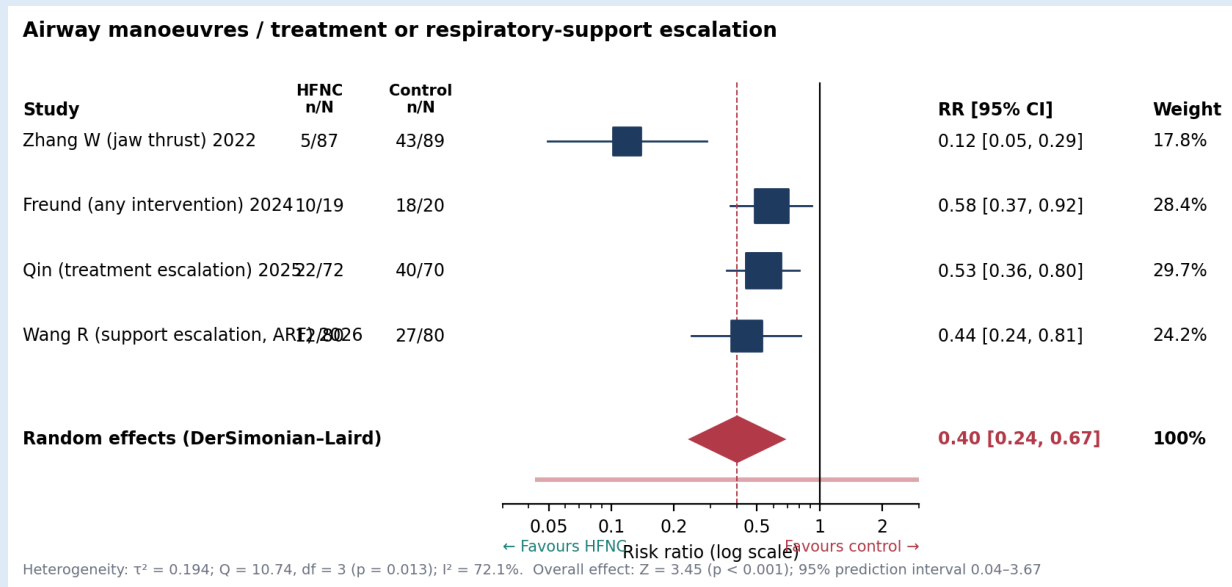


Figure 21. Forest plot of airway manoeuvres, predefined interventions or escalation of respiratory support.^{9,38,47,48}

Severe Hypoxaemia and Advanced Airway Rescue

Three RCTs (456 participants) reported severe hypoxaemic events or advanced rescue (bag-mask ventilation, severe desaturation, intubation within 24 h): 9 of 224 (4.0%) versus 35 of 232 (15.1%) (RR 0.31, 0.16–0.63; $I^2 = 0\%$), i.e. 104 fewer events per 1,000. Of note, intubation within 24 h in ARF fell from 20.0% to 7.5%. This composite is clinically heterogeneous and should be interpreted as hypothesis-supporting.^{15,38,47}

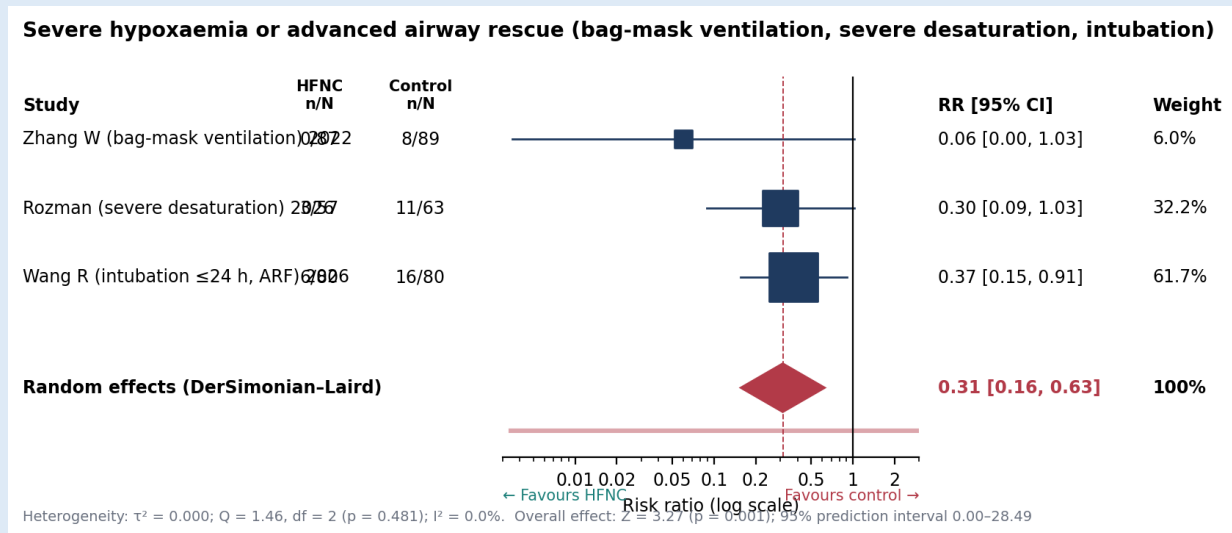


Figure 22. Forest plot of severe hypoxaemia or advanced airway rescue.^{15,38,47}

Flow–Response Relationship

In the six-arm flow trial, desaturation under propofol sedation fell monotonically from 42.5% at 10 L/min to 17.5%, 15.0%, 10.0%, 2.5% and 0% at 20, 30, 40, 50 and 60 L/min, respectively; probit regression by the investigators estimated an ED₉₅ of 43.2 L/min (95% CI 36.4–56.0). Our logistic model on the same arm-level data gave a slope of -0.077 per L/min (OR 0.47 per 10 L/min increase), predicting desaturation risks of 40% at 10 L/min, 6% at 40 L/min and 1.4% at 60 L/min. The four-arm deep-sedation trial reproduced this gradient (57.1% with 5 L/min nasal cannula vs. 16.9%, 12.0% and 5.0% at 25, 45 and 65 L/min), and an IPD meta-analysis reported that flows ≥ 45 L/min were associated with lower desaturation risk (OR 0.28).^{11,37,63}

Table 11. Arm-level flow–response data.

Study	Arm (flow)	Desaturation n/N	Incidence (%)	Model- predicted (%)
Zhang W 2024 ¹¹	10 L/min	17/40	42.5	40.2
	20 L/min	7/40	17.5	24.2
	30 L/min	6/40	15.0	12.9
	40 L/min	4/40	10.0	6.3
	50 L/min	1/40	2.5	3.0
	60 L/min	0/40	0.0	1.4
Wang M 2026 ³⁷	Nasal cannula 5 L/min	48/84	57.1	—

	HFNC 25 L/min	14/83	16.9	—
	HFNC 45 L/min	10/83	12.0	—
	HFNC 65 L/min	4/80	5.0	—

Model-predicted values derived in this review from a maximum-likelihood logistic regression (intercept 0.369; slope -0.0766 per L/min) fitted to Zhang W 2024. Counts for Wang M 2026 were back-calculated from reported percentages and analysed sample ($n = 330$) and are internally consistent.

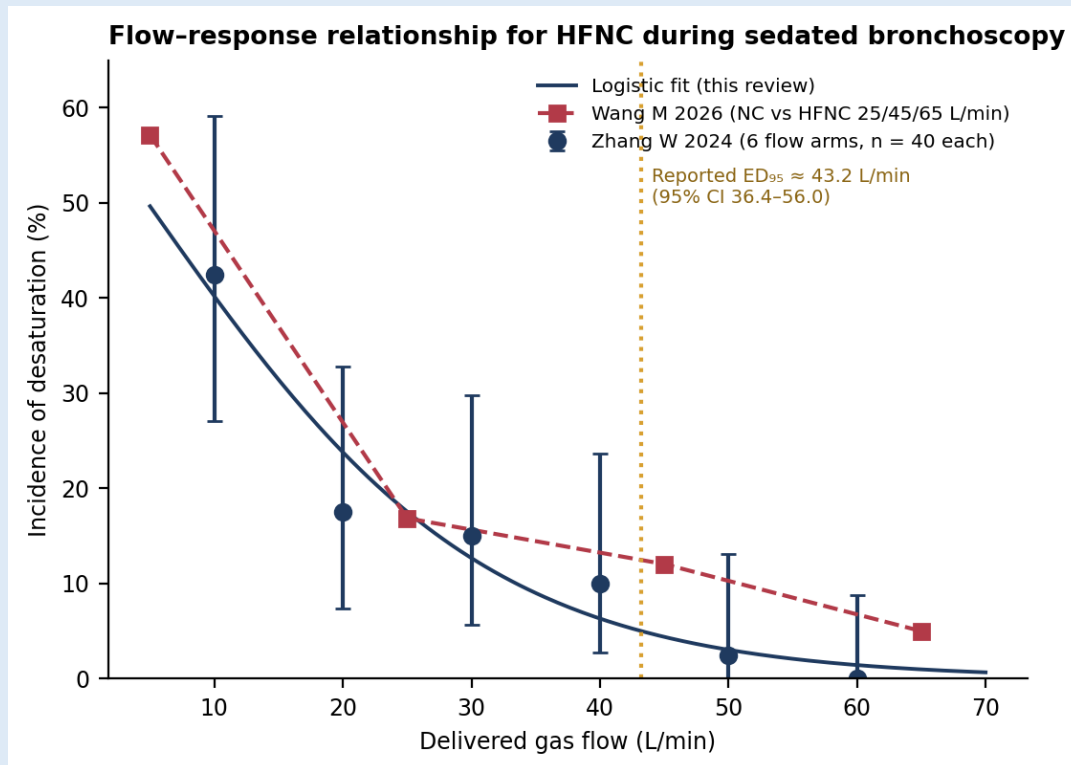


Figure 23. Flow–response relationship: observed desaturation incidence (exact 95% CI) across six HFNC flows with fitted logistic curve (Zhang W 2024), overlaid with the four-arm deep-sedation trial (Wang M 2026). The dotted line marks the reported ED_{95} .^{11,37}

HFNC Versus Non-Invasive Ventilation

Two RCTs (91 patients) compared HFNC with NIV in hypoxaemic patients. In critically ill patients with ARF, oxygenation was higher with NIV before, during and after bronchoscopy, two HFNC patients could not proceed because of progressive hypoxaemia and one required NIV rescue, while 24-hour intubation rates did not differ (3 vs. 1). In patients with $PaO_2 < 70$ mmHg, desaturation

below 90% tended to be more frequent with HFNC (RR 2.88, 0.88–9.44), and NIV better preserved PaO₂ when baseline PaO₂ was < 60 mmHg. These data define a boundary: HFNC is effective in mild-to-moderate hypoxaemia but NIV/CPAP remains preferable in more severe ARF.^{2,12,13}

Special Populations

Children: in 104 children aged 1 month–16 years, HFNC reduced hypoxaemia (SpO₂ < 94%) with an absolute risk reduction of 27% and NNT of 3.75, most markedly during BAL, without a difference in severe hypoxaemia. **COPD:** in PROSA-2, HFNC halved cumulative hypoxaemia time (1.8% vs. 3.8%) and hypoxaemic events. **Lung transplantation:** HFNC eliminated procedure interruptions during TBLB. **Airway stenosis/obesity:** in high-risk nasal bronchoscopy, HFNC reduced desaturation, interruption and escalation, and lowered peak PtcCO₂. **Hypoxaemic ARF:** HFNC via a single-prong interface reduced escalation and intubation, and observational data suggest stable SpO₂ during BAL. **Rigid bronchoscopy:** during apnoea under general anaesthesia, HFNC attenuated the PaO₂ decline and reduced interruptions without changing nadir SpO₂.^{9,10,38,42,46,49,53}

Physiological, Procedural and Patient-Centred Secondary Outcomes

Table 12. Secondary physiological, procedural and patient-centred outcomes.

Domain	Evidence (studies)	Summary of findings
Arterial oxygenation	Lucangelo 2012; Longhini 2022; Yue 2025; Kim HJ 2024 ^{16,44,49,51}	HFNC preserved PaO ₂ (e.g., 11.1 vs 9.1 kPa at end of BAL), with a flow-dependent effect (60 > 40 L/min)
Carbon dioxide	Qin 2025; Wang M 2026; Yue 2025; Gupta 2025; Takakuwa 2018 ^{9,37,50–52}	No increase in hypercapnia; lower peak PtcCO ₂ /PaCO ₂ in several trials, consistent with dead-space washout
Lung volume and respiratory mechanics	Longhini 2022; Wang R 2026 ^{16,38}	EIT showed preserved EELI and smaller loss of tidal impedance; less diaphragm activation
Respiratory and heart rate	Wang R 2021; Burton 2025 ^{8,14}	Lower respiratory and heart rates during bronchoscopy with HFNC
Procedure duration and conduct	Wang R 2021; Qin 2025; Ben-Menachem 2020 ^{8,9,42}	Shorter procedures, fewer interruptions and withdrawals
Complications	Wang R 2021; Luo 2024; Sehgal 2025 ^{8,36,59}	Less agitation, supraventricular tachycardia and pneumothorax in the largest RCT; fewer general adverse events in a hypoxaemic cohort; no excess complications

Comfort and satisfaction	Yilmazel Ucar 2021; Sehgal 2025; Darie 2025; Burton 2025; Wang M 2026 ^{10,14,36,37,41}	Comfort better or unchanged; clinician/anaesthetist satisfaction higher; > 97% willing to repeat under deep sedation
--------------------------	---	--

Summary of Pooled Effects, Absolute Effects and Certainty of Evidence

Table 13. Summary of all quantitative syntheses.

Outcome	k	N	HFNC events	Control events	Effect (95% CI)	I ² (%)	95% PI	p
Desaturation (RR)	12	2,318	185/1,234	432/1,084	RR 0.34 (0.25–0.47)	71.7	0.12–0.95	< 0.001
Desaturation (OR; RCT + observational)	15	3,234	—	—	OR 0.20 (0.14–0.28)	61.7	0.06–0.61	< 0.001
Nadir SpO ₂ (RCTs)	5	1,083	—	—	MD +4.95 (2.89–7.00)	83.6	–2.39 to 12.29	< 0.001
Procedure interruption	4	1,059	59/527	160/532	RR 0.39 (0.28–0.54)	12.5	0.16–0.94	< 0.001
Airway manoeuvre / escalation	4	517	49/258	128/259	RR 0.40 (0.24–0.67)	72.1	0.04–3.67	< 0.001
Severe hypoxaemia / advanced rescue	3	456	9/224	35/232	RR 0.31 (0.16–0.63)	0.0	NE	0.001

MD, mean difference (percentage points); NE, not estimable/uninformative with three studies; PI, prediction interval.

Table 14. Meta-analysis data by outcome category (Author / Year / Effect / Lower CI / Upper CI).

Author	Year	Effect	Lower CI	Upper CI
Desaturation — risk ratio				
Douglas	2018	0.40	0.14	1.14
Ben-Menachem	2020	0.23	0.11	0.50
Yilmazel Ucar	2021	0.19	0.08	0.48
Wang R	2021	0.43	0.32	0.59
Longhini	2022	0.20	0.05	0.79
Zhang W	2022	0.16	0.06	0.43
Freund	2024	0.29	0.14	0.63
Qin	2025	0.57	0.39	0.82
Sehgal	2025	0.47	0.32	0.68
Yue	2025	0.20	0.05	0.84
Wang M	2026	0.20	0.13	0.30
Rozman	2026	0.77	0.53	1.10
Desaturation — odds ratio (additional studies)				
Luo	2024	0.19	0.06	0.64
Nilushi	2022	0.07	0.02	0.32
Darie	2025	0.20	0.12	0.31

Nadir SpO ₂ — mean difference				
Wang R	2021	3.60	3.11	4.09
Douglas	2018	5.17	2.77	7.56
Qin	2025	6.50	3.36	9.64
Kim HJ	2024	1.67	-0.20	3.54
Irfan	2021	9.20	6.44	11.96
de Vico	2025	8.20	0.89	15.51
Procedure interruption — risk ratio				
Ben-Menachem	2020	0.06	0.00	0.92
Wang R	2021	0.39	0.27	0.54
Kim HJ	2024	0.13	0.02	0.97
Qin	2025	0.45	0.29	0.69
Airway manoeuvre / escalation — risk ratio				
Zhang W	2022	0.12	0.05	0.29
Freund	2024	0.58	0.37	0.92
Qin	2025	0.53	0.36	0.80
Wang R	2026	0.44	0.24	0.81
Severe hypoxaemia / advanced rescue — risk ratio				
Zhang W	2022	0.06	0.00	1.03
Rozman	2026	0.30	0.09	1.03
Wang R	2026	0.37	0.15	0.91

Values are study-level effect estimates with 95% confidence limits as entered into the meta-analyses.

Applying the pooled RR to a range of baseline risks shows that the absolute benefit rises steeply with baseline risk (Table 16): from 66 fewer desaturations per 1,000 procedures (NNT $\approx$ 15) when control risk is 10%, to 262 fewer (NNT $\approx$ 4) at the pooled control risk of 40%, and 394 fewer (NNT $\approx$ 2.5) when control risk is 60%, as observed in high-risk and deep-sedation cohorts.^{9,37,48}

Table 15. Absolute effects of HFNC on desaturation according to baseline (control) risk.

Baseline risk with conventional O ₂	Expected with conventional O ₂ (per 1,000)	Expected with HFNC (per 1,000)	Difference (95% CI) per 1,000	NNT
10% (low risk, topical anaesthesia)	100	34	66 fewer (53–75 fewer)	15
20%	200	69	131 fewer (106–150 fewer)	8
30%	300	103	197 fewer (159–225 fewer)	5
40% (pooled control risk of included RCTs)	400	138	262 fewer (212–299 fewer)	4

60% (high-risk / deep sedation)	600	206	394 fewer (318–449 fewer)	3
---------------------------------	-----	-----	---------------------------	---

Calculated from the pooled RR 0.34 (95% CI 0.25–0.47). NNT, number needed to treat to prevent one desaturation (rounded up).

Table 16. GRADE summary of findings: HFNC compared with conventional oxygen (or NIV) during bronchoscopy.

Outcome (studies; participants)	Relative effect (95% CI)	Absolute effect	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Certainty
Desaturation (12 RCTs; 2,318)	RR 0.34 (0.25–0.47)	262 fewer per 1,000	Serious*	Not serious†	Not serious	Not serious	Undetected‡	⊕⊕⊕○ Moderate
Nadir SpO ₂ (5 RCTs; 1,083)	—	MD 4.95 higher (2.89–7.00)	Serious*	Serious (I ² 84%)	Not serious	Not serious	Undetected	⊕⊕○○ Low
Procedure interruption (4 RCTs; 1,059)	RR 0.39 (0.28–0.54)	183 fewer per 1,000	Serious*	Not serious	Not serious	Not serious	Not assessable	⊕⊕⊕○ Moderate
Airway manoeuvre / escalation (4 RCTs; 517)	RR 0.40 (0.24–0.67)	296 fewer per 1,000	Serious*	Serious (I ² 72%)	Not serious	Not serious	Not assessable	⊕⊕○○ Low
Severe hypoxaemia / advanced rescue (3 RCTs; 456)	RR 0.31 (0.16–0.63)	104 fewer per 1,000	Serious*	Not serious	Serious (composite)	Not serious	Not assessable	⊕⊕○○ Low
HFNC vs NIV, hypoxaemic ARF (2 RCTs; 91)	RR 2.88 (0.88–9.44)§	Favours NIV	Not serious	Not serious	Not serious	Very serious	Not assessable	⊕⊕○○ Low

Desaturation, observational (2 studies; 316)	OR 0.13 (0.05–0.33)	—	Serious (ROBINS-I)	Not serious	Not serious	Serious	Not assessable	⊕○○○ Very low
--	---------------------	---	--------------------	-------------	-------------	---------	----------------	------------------

*Open-label delivery with discretionary co-interventions; most trials at "some concerns".

†Downgrading not applied because all trials favoured HFNC and the prediction interval excluded the null.

‡Egger $p = 0.08$; large trials concordant. §Single trial with event data (Saksitthichok

2019), RR for $SpO_2 < 90\%$ with HFNC vs NIV.

GRADE certainty of evidence by outcome

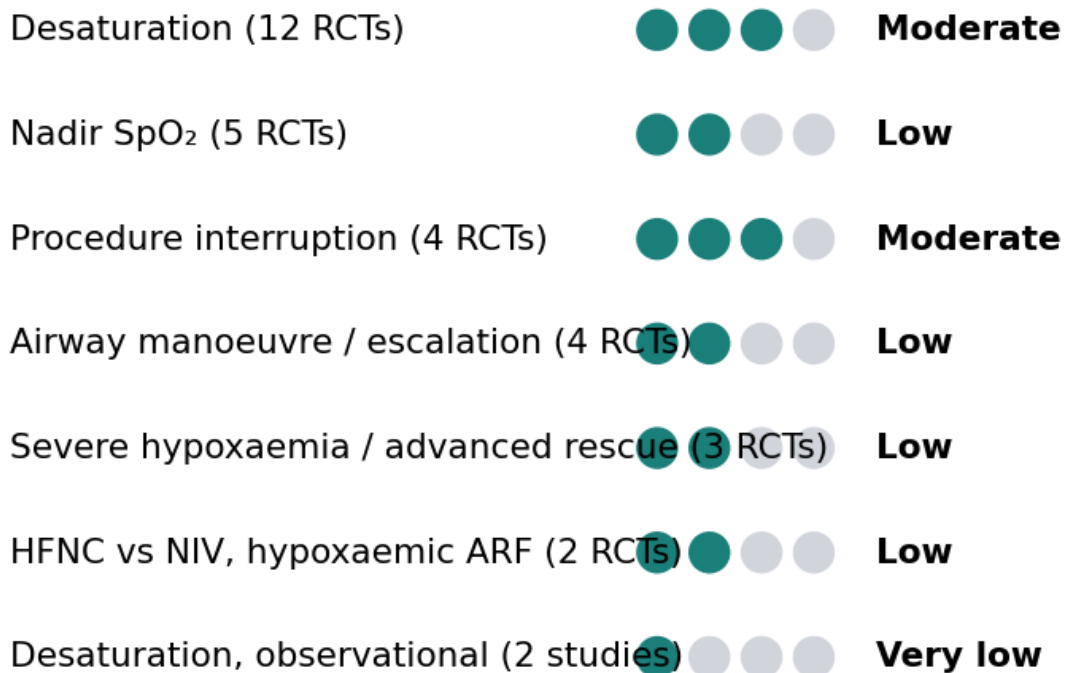


Figure 24. Visual summary of GRADE certainty of evidence by outcome.⁴⁰

DISCUSSION

Summary of Principal Findings

This systematic review of 32 primary studies (4,572 participants) published during the last 15 years provides consistent evidence that HFNC during bronchoscopy is associated with better maintenance of SpO₂. In adult RCTs, HFNC reduced the risk of desaturation by approximately 66% (RR 0.34), increased nadir SpO₂ by about 5 percentage points and reduced procedure interruptions by 61%, airway manoeuvres or escalation by 60% and severe hypoxaemia or advanced rescue by 69%. The prediction interval for the primary outcome excluded the null, the effect was robust across seven sensitivity analyses and all subgroups, and observational evidence was concordant. A clear flow–response gradient strengthens the causal interpretation, while trials in moderate-to-severe hypoxaemic respiratory failure indicate that NIV provides superior oxygenation in that specific population. Accordingly, the primary hypothesis (H₁) is accepted, the null hypothesis is rejected, and the secondary hypotheses regarding nadir SpO₂, interruptions, flow dependence and the HFNC–NIV boundary are supported.^{8,11–13,36,37}

Physiological Interpretation

The magnitude and pattern of benefit are coherent with HFNC physiology. First, delivering flows that approach or exceed peak inspiratory flow minimises entrainment of room air, so the delivered FiO₂ approximates the set FiO₂ even during tachypnoea, coughing and mouth breathing induced by the bronchoscope. The observation that the FiO₂-matched EBUS trial found a smaller and non-significant reduction in "any" desaturation, but significantly fewer severe and persistent desaturations and a higher nadir SpO₂, suggests that a considerable part—though not all—of the benefit derives from superior and more stable oxygen delivery rather than from FiO₂ alone.^{3,9,15}

Second, HFNC generates a modest, flow-dependent positive airway pressure and preserves EELV. Electrical impedance tomography during BAL demonstrated a fall of approximately 200 mL in end-expiratory lung impedance with standard therapy that was abolished by HFNC at 60 L/min, together with less diaphragmatic activation; in ARF, the single-prong interface attenuated both tidal and end-expiratory impedance losses. These data explain why HFNC is particularly protective during

suction and BAL, which are the most de-recruiting phases of the procedure, and why a BAL volume > 60 mL and a low FVC predicted residual desaturation despite HFNC.^{8,16,25,38}

Third, washout of the nasopharyngeal dead space improves ventilatory efficiency and may offset sedation-related hypoventilation. Bench and volunteer studies show CO₂ clearance at relatively low flows with the mouth open, reduced minute ventilation at stable PaCO₂ and a flow-dependent reduction of respiratory rate; asymmetrical nasal occlusion—analogue to the bronchoscope occupying one nostril—may further enhance clearance. Clinically, this translated into equal or lower transcutaneous and arterial CO₂ with HFNC across trials, allaying concerns about masked hypoventilation.^{9,24,26–28,51}

Finally, apnoeic or "mass-flow" oxygenation maintains alveolar oxygen delivery during transient apnoea, which may explain the striking effects under deep propofol sedation and the attenuated PaO₂ decline during apnoeic rigid bronchoscopy. Heated humidification preserves mucociliary function and comfort, which may explain less agitation and fewer arrhythmias in the largest trial.^{8,37,49,64,65}

Comparison with Previous Systematic Reviews and Meta-Analyses

Our estimates are congruent with, but more comprehensive than, prior syntheses (Table 18). Early reviews of five to nine RCTs reported RRs of 0.25–0.34 for hypoxaemic events and higher nadir SpO₂ (MD 4.3–7.1). Broader procedural-sedation meta-analyses including gastrointestinal endoscopy found similar relative effects (RR 0.32–0.37). The most recent 2026 reviews, including 11–17 RCTs, reported RR 0.39–0.41 or OR 0.23, and an IPD meta-analysis suggested greater relative benefit in patients with lower body-mass index and lower baseline respiratory and heart rates, and with flows $\geq$ 45 L/min. A review focused on high-risk patients (five RCTs) reported an OR of 0.14. Our review extends this literature by adding non-randomised evidence under ROBINS-I, prediction intervals, a flow–response model, absolute effects across baseline risks and a formal exploration of heterogeneity that identified FiO₂ matching and extreme flow/deep sedation as its principal drivers.^{29–35,63,66,67}

Table 17. Comparison of the present review with previous systematic reviews and meta-analyses (discussion only; not part of the evidence base).

Review	Scope	Studies (participants)	Principal estimate for hypoxaemia	Other findings
Su 2021 ²⁹	Bronchoscopy, RCTs	5 (257)	RR 0.25 (0.14–0.42)	Lowest SpO ₂ WMD 7.12; PaO ₂ higher
Sampsonas 2022 ³⁰	Bronchoscopy incl. EBUS, RCTs	6 (1,170)	Fewer hypoxaemic events	Fewer interruptions and pneumothoraces
Roy 2022 ³¹	HFNC vs any device incl. NIV	9 (1,306)	RR 0.34 (0.27–0.44)	Nadir MD 4.30; NIV better nadir SpO ₂
Tao 2022 ³²	Bronchoscopy + GI endoscopy	15 (4,093)	RR 0.32 (0.22–0.47)	Fewer airway interventions and interruptions
Thiruvengkatarajan 2022 ⁶⁶	Procedural sedation (all)	19 (4,121)	RR 0.37 (0.24–0.56)	Nadir MD 4.1; no effect on hypercarbia
Wei 2024 ³³	Transnasal HFNC, bronchoscopy	12 (1,631)	RR 0.27 (0.18–0.41)	NIV superior to HFNC; shorter procedures
Nishie 2026 ³⁴	Adults, RCTs	11 (1,714)	RR 0.39 (0.26–0.59)	Interruption RR 0.39; nadir MD 4.5
Fliess de Castro 2026 ³⁵	Adults, RCTs	14 (2,480)	RR 0.41 (0.29–0.59)	Nadir MD 5.10; sedation use slightly higher
Wang W 2026 ⁶⁷	High-risk patients, RCTs	5 (1,054)	OR 0.14 (0.08–0.27)	Interruption OR 0.18
Wang J 2026 (IPD) ⁶³	Adults, RCTs + IPD	17 (3,116)	OR 0.23 (0.15–0.34)	Benefit modifiers: BMI, RR, HR; flow $\geq$ 45 L/min
Present review	RCTs + observational, 2011–2026	32 (4,572)	RR 0.34 (0.25–0.47); OR 0.20	PI 0.12–0.95; NNT 3.8; flow–response; GRADE moderate

BMI, body-mass index; GI, gastrointestinal; HR, heart rate; IPD, individual participant data; PI, prediction interval; RR (in "Other findings"), respiratory rate; WMD, weighted mean difference.

Interpreting Heterogeneity and Neutral Trials

Heterogeneity in this field is expected and informative rather than disqualifying. Control-arm risks ranged from 25% to 90%, sedation from topical anaesthesia to deep propofol sedation, oxygen routes from oral to transnasal, and desaturation definitions from any momentary reading below 90% to sustained desaturation for 30 s. Neutral or partially neutral trials share recognisable features: conscious rather than deep sedation with a low baseline event rate, deliberate matching of nominal FiO_2 , or unconventional outcome definitions such as a 3% fall from baseline. In the Australian pragmatic trial, time with $\text{SpO}_2 < 90\%$ was low in both arms, limiting the scope for improvement, yet HFNC reduced respiratory rate during EBUS and improved clinician satisfaction. Similarly, the Indian EBUS trial found no overall difference but a large benefit in patients with cardiopulmonary comorbidity or baseline $\text{SpO}_2 < 97\%$. These findings support a risk-stratified rather than universal application of HFNC.^{7,14,15,50}

Flow Rate, Interface and Route

The flow–response data are among the most clinically actionable findings. Desaturation fell steeply between 10 and 40 L/min and approached zero at 50–60 L/min under propofol sedation, with an ED_{95} of approximately 43 L/min; IPD analyses independently associated flows ≥ 45 L/min with lower risk. Flows of 50–60 L/min, titrated upward to 70–80 L/min in COPD or when desaturation occurs, are therefore rational. For transnasal bronchoscopy, a single-prong cannula in the contralateral nostril preserved high-flow delivery and generated a higher positive pressure in bench testing, and was effective both in stable inpatients and in ARF. With the oral route, the open mouth reduces airway pressure but dead-space washout remains effective, and bite-block or oral approaches still benefited from HFNC.^{8,10,11,26,38,57,63}

Sedation Depth and Anaesthetic Practice

International sedation recommendations diverge regarding sedation depth, sedative agents, the qualification of the sedating clinician and oxygen supplementation. Our subgroup analysis suggests that HFNC is beneficial across sedation strategies, but the absolute benefit is greatest under deep sedation, where control-arm desaturation reached 29–57% and jaw thrust was needed in almost half of patients with face-mask oxygen. HFNC may thus enable deep sedation without an advanced

airway, as shown by the absence of laryngeal-mask or intubation requirements in the four-arm trial, and may be positioned as an alternative to a supraglottic airway in selected EBUS procedures. Nevertheless, HFNC does not replace vigilant airway management: in a large series of deeply sedated EBUS procedures, obesity was the key predictor of HFNC failure, highlighting upper-airway obstruction as a mechanism that high flow cannot overcome without airway manoeuvres.^{18,19,37,47,48,58,68}

High-Risk Populations and the Boundary with NIV

Patients with COPD, obesity/OSA, lung transplantation, central airway stenosis or pre-existing hypoxaemia derive the largest absolute benefit because their baseline risk is highest. Meta-analytic evidence in obese perioperative patients is mixed, but in bronchoscopy-specific high-risk cohorts HFNC reduced desaturation, interruption and treatment escalation. In patients with established moderate-to-severe hypoxaemic ARF, however, the positive end-expiratory pressure delivered by NIV or CPAP is substantially higher and more reliable than that generated by HFNC; two RCTs and a pooled review consistently favoured NIV for oxygenation in this group. A pragmatic threshold consistent with the evidence is to prefer NIV/CPAP when PaO₂ on room air is < 60 mmHg or the PaO₂/FiO₂ ratio is severely reduced, reserving HFNC for mild-to-moderate hypoxaemia or when NIV is not tolerated, with ICU or anaesthesia backup.^{2,9,10,12,13,17,42,69,70}

Clinical Significance of Preserving SpO₂

Whether reductions in transient desaturation translate into patient-important outcomes has been questioned. Several lines of evidence suggest that they do: intraprocedural SpO₂ ≤ 94% is independently associated with post-bronchoscopy respiratory adverse events; HFNC reduced procedure interruptions, agitation, supraventricular tachycardia and pneumothorax in the largest trial; and in ARF it reduced escalation of respiratory support and intubation within 24 hours. Shorter and uninterrupted procedures may also improve diagnostic yield and throughput. These downstream benefits, however, were secondary outcomes in most trials and require confirmation.^{1,8,21,38}

Safety, Resource Use and Implications for Middle-Income Settings

No trial reported HFNC-specific serious adverse events, and CO₂ retention was not increased. Resource considerations include device cost, oxygen consumption at high flows and single-use

circuits. In middle-income health systems, including Indonesia, where bronchoscopy and EBUS services are expanding and anaesthesia-led deep sedation is not universally available, the absolute-effect estimates allow targeted deployment: at a 10% baseline risk, 15 patients must be treated to prevent one desaturation, whereas in high-risk or deeply sedated patients (baseline risk $\geq 40\text{--}60\%$), only three to four need to be treated. Prioritising HFNC for these groups, together with standardised training in airway manoeuvres and escalation, is likely to be the most efficient strategy. The ongoing OxyFOB cohort will provide real-world data on practice variation and outcomes across European centres.^{9,19,37,39}

Evidence-Informed Clinical Pathway

Integrating the pooled effects, subgroup findings, flow–response data and the HFNC–NIV boundary, we propose a risk-stratified pathway (Figure 26): pre-procedural stratification; conventional oxygen as an acceptable option for low-risk patients under topical anaesthesia; HFNC at $\geq 45\text{--}60$ L/min with titrated FiO₂ for moderate-to-high-risk patients, sedated or prolonged procedures, BAL, TBLB and EBUS; NIV/CPAP for established moderate-to-severe hypoxaemic ARF; and a stepwise rescue algorithm. This pathway is derived from the evidence synthesised here and should be validated prospectively.^{1,11,12,17}

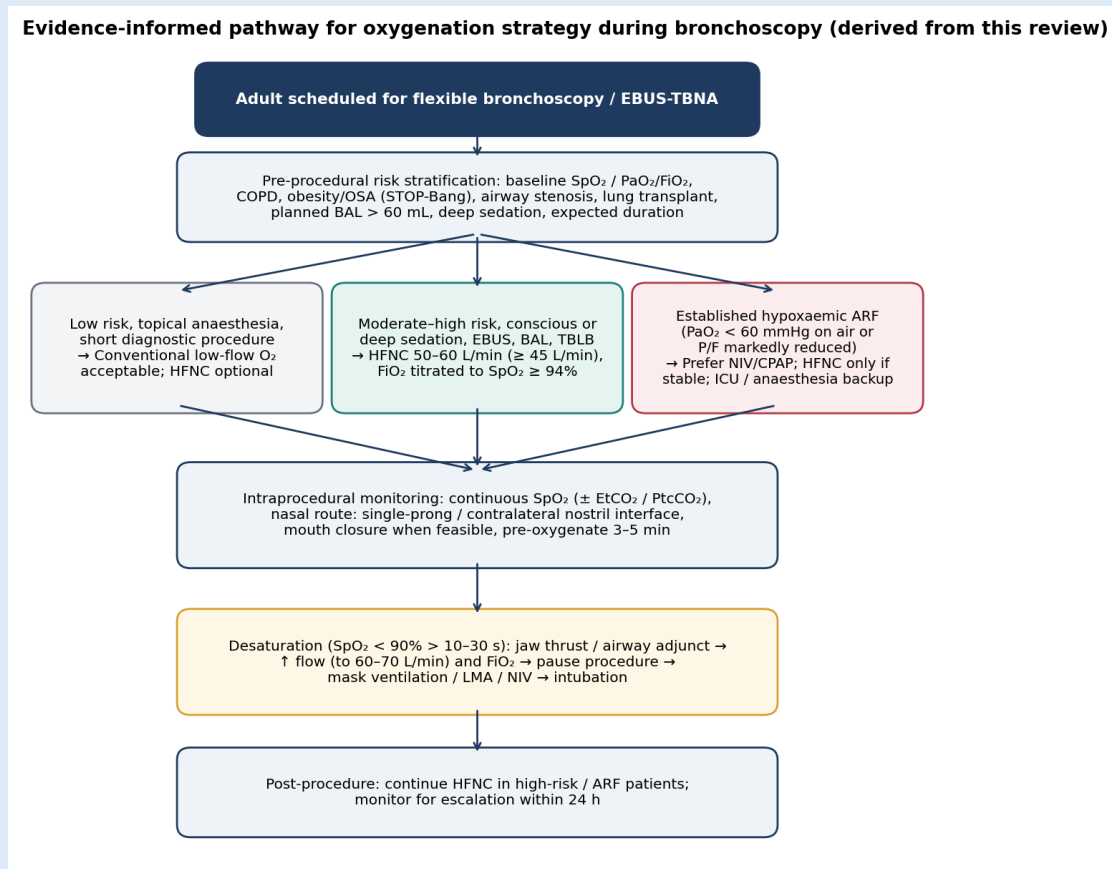


Figure 25. Evidence-informed, risk-stratified pathway for the selection of oxygenation strategy during bronchoscopy, derived from the findings of this review. ARF, acute respiratory failure; CPAP, continuous positive airway pressure; EtCO₂, end-tidal CO₂; LMA, laryngeal mask airway; PtcCO₂, transcutaneous CO₂.^{1,8,11–13}

Strengths

Strengths include the restriction to contemporary evidence (2011–2026) including the complete 2025–2026 trial generation; integration of randomised and non-randomised evidence with design-appropriate risk-of-bias tools; verification of every included record and of arm-level data against publisher or PubMed Central sources; conservative random-effects modelling complemented by prediction intervals and multiple estimators; extensive sensitivity, subgroup, meta-regression and cumulative analyses; a flow–response model; translation into absolute effects; and GRADE assessment.^{4–6,40}

Research Gaps and Recommendations for Future Studies

Table 18. Remaining research gaps and recommended design features for future trials.

Research gap	Recommended design / action
Heterogeneous desaturation definitions	Adopt a core outcome set: SpO ₂ < 90% for > 10 s, severe desaturation (< 80% or < 90% for > 60 s), cumulative hypoxaemia time and nadir SpO ₂ captured automatically
Unblinded outcome assessment and discretionary rescue	Automated continuous data capture, blinded adjudication and protocolised rescue algorithms
Uncertain contribution of FiO ₂ vs flow	Factorial trials crossing flow (high vs low) with matched FiO ₂
Limited patient-important endpoints	Power trials for post-procedural respiratory adverse events, diagnostic yield, unplanned admission and cost-effectiveness
Few data in severe hypoxaemic ARF, obesity and children	Multicentre RCTs of HFNC vs NIV/CPAP stratified by PaO ₂ /FiO ₂ ; adequately powered paediatric and obese cohorts
Optimal flow in different routes and interfaces	Dose-finding trials for oral vs nasal routes, single- vs dual-prong interfaces and COPD
Evidence from low- and middle-income countries	Pragmatic trials and registries in settings with limited anaesthesia support, including South-East Asia

CONCLUSIONS AND RECOMMENDATIONS

Conclusions

Across 32 primary studies and 4,572 participants published between 2012 and 2026, the use of high-flow nasal cannula during bronchoscopy was associated with superior maintenance of peripheral oxygen saturation. HFNC reduced the risk of intraprocedural desaturation by approximately two-thirds (RR 0.34; NNT $\approx$ 4 at average baseline risk), raised nadir SpO₂ by about 5 percentage points and reduced procedure interruptions, airway rescue manoeuvres and severe hypoxaemic events, with a consistent flow–response relationship and no signal of harm. The certainty of evidence is moderate for desaturation and procedure interruption and low for other outcomes. In established moderate-to-severe hypoxaemic respiratory failure, NIV/CPAP provides better oxygenation than HFNC.^{8,10–13,36}

Recommendations

For clinical practice: (1) perform pre-procedural risk stratification for hypoxaemia in every patient; (2) use HFNC at $\geq$ 45–60 L/min, with FiO₂ titrated to SpO₂ $\geq$ 94%, for sedated, prolonged or BAL/TBLB/EBUS procedures and in high-risk patients (COPD, obesity/OSA, lung transplantation,

airway stenosis, mild-to-moderate hypoxaemia); (3) consider a single-prong interface for transnasal bronchoscopy; (4) prefer NIV/CPAP in moderate-to-severe hypoxaemic ARF; and (5) maintain continuous oximetry, CO₂ monitoring where feasible and a protocolised rescue algorithm.^{1,2,8,38}

For institutions and policy makers: include HFNC devices and training in bronchoscopy-suite standards, prioritising high-risk and deep-sedation lists to maximise absolute benefit in resource-constrained settings. **For researchers:** conduct adequately powered, multicentre trials with standardised outcome definitions, automated blinded outcome capture, matched-FiO₂ or factorial designs and patient-important endpoints, including trials in low- and middle-income countries and in children.^{19,39,63}

DECLARATIONS

Funding: none. **Conflicts of interest:** the authors declare no competing interests. **Data availability:** extracted study-level data and analytic code are available from the corresponding author on reasonable request.

REFERENCES

1. Du Rand IA, Blaikley J, Booton R, Chaudhuri N, Gupta V, Khalid S, et al. British Thoracic Society guideline for diagnostic flexible bronchoscopy in adults: accredited by NICE. *Thorax*. 2013;68 Suppl 1:i1–44. doi:10.1136/thoraxjnl-2013-203618. Available from: https://consensus.app/papers/details/f5319191d66b51378ae4d3190f7a24db/?utm_source
2. Pelaia C, et al. Oxygenation strategies during flexible bronchoscopy: a review of the literature. *Respir Res*. 2021;22(1):253. doi:10.1186/s12931-021-01846-1. Available from: https://consensus.app/papers/details/f4f7c4738aac53858f8e3a519b6877f7/?utm_source
3. Li J, et al. The effects of flow settings during high-flow nasal cannula support for adult subjects: a systematic review. *Crit Care*. 2023. doi:10.1186/s13054-023-04361-5. Available from: https://consensus.app/papers/details/32ad23d981505400935c1dbcbad0315d/?utm_source
4. Page MJ, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Syst Rev*. 2021;10(1):89. doi:10.1186/s13643-021-01626-4. Available from: https://consensus.app/papers/details/c1a1d4c752e857f2ba6639ed813f181a/?utm_source

5. Sterne JAC, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:l4898. doi:10.1136/bmj.l4898. Available from: https://consensus.app/papers/details/99eca47c80a253ec80ec043138089451/?utm_source
6. Sterne JA, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355:i4919. doi:10.1136/bmj.i4919. Available from: https://consensus.app/papers/details/87e695ba99c35aea9a306d7410d8d111/?utm_source
7. Douglas N, Ng I, Nazeem F, Lee K, Mezzavia P, Krieser R, et al. A randomised controlled trial comparing high-flow nasal oxygen with standard management for conscious sedation during bronchoscopy. *Anaesthesia*. 2018;73(2):169–76. doi:10.1111/anae.14156. Available from: https://consensus.app/papers/details/54da56d1f44d54eda10defe5ff488a46/?utm_source
8. Wang R, Li HC, Li XY, Tang X, Chu HW, Yuan X, et al. Modified high-flow nasal cannula oxygen therapy versus conventional oxygen therapy in patients undergoing bronchoscopy: a randomized clinical trial. *BMC Pulm Med*. 2021;21(1):367. doi:10.1186/s12890-021-01744-8. Available from: https://consensus.app/papers/details/203f08d4550855809c29714ad63dd294/?utm_source
9. Qin H, Li J, Wang J, et al. Comparison of high-flow nasal cannula and conventional oxygen therapy for high-risk patients during bronchoscopy examination: a multi-center randomized controlled trial. *Ann Am Thorac Soc*. 2025;22(7):1018–26. doi:10.1513/AnnalsATS.202410-1109OC. Available from: https://consensus.app/papers/details/2c5b8e9aedc25f12b8cfc5a5fed1b6d0/?utm_source
10. Darie AM, et al. Preventing oxygen desaturation during bronchoscopy in COPD patients using high-flow oxygen versus standard management: the randomised controlled PROSA 2 trial. *Eur Respir J*. 2025. doi:10.1183/13993003.01586-2024. Available from: https://consensus.app/papers/details/2547df55bde45862b2c1063105391e7f/?utm_source
11. Zhang W, Yuan X, Shen Y, Wang J, Xie K, Chen X. Optimal flow of high-flow nasal cannula oxygenation to prevent desaturation during sedation for bronchoscopy: a randomized controlled study. *Ther Adv Respir Dis*. 2024;18:17534666241246637. doi:10.1177/17534666241246637. Available from: https://consensus.app/papers/details/4c00129d6d31549598519a617a24cb94/?utm_source

12. Simon M, Braune S, Frings D, Wiontzek AK, Klose H, Kluge S. High-flow nasal cannula oxygen versus non-invasive ventilation in patients with acute hypoxaemic respiratory failure undergoing flexible bronchoscopy – a prospective randomised trial. Crit Care. 2014;18(6):712. doi:10.1186/s13054-014-0712-9. Available from: https://consensus.app/papers/details/f699316f8de35685831edb30082cf649/?utm_source
13. Saksitthichok B, Petnak T, So-Ngern A, Boonsarngsuk V. A prospective randomized comparative study of high-flow nasal cannula oxygen and non-invasive ventilation in hypoxemic patients undergoing diagnostic flexible bronchoscopy. J Thorac Dis. 2019;11(5):1929–39. doi:10.21037/jtd.2019.05.02. Available from: https://consensus.app/papers/details/7ea118207d955c75bcb59d18d68dc721/?utm_source
14. Burton G, et al. High flow nasal oxygen and low flow oxygen are equally effective in providing oxygenation during bronchoscopy under conscious sedation: a randomised controlled trial. Respirology. 2025. doi:10.1111/resp.70051. Available from: https://consensus.app/papers/details/068ecc4120c95abea4cf690e264650c4/?utm_source
15. Rozman A, et al. High-flow versus conventional nasal oxygen during EBUS-TBNA under matched nominal FiO₂: a multicenter randomized controlled trial. ERJ Open Res. 2026. doi:10.1183/23120541.00693-2026. Available from: https://consensus.app/papers/details/5ce1da4b8a0c5fbc9852561e38fe28e8/?utm_source
16. Longhini F, Pelaia C, Garofalo E, Bruni A, Placida R, Iaquina C, et al. High-flow nasal cannula oxygen therapy for outpatients undergoing flexible bronchoscopy: a randomised controlled trial. Thorax. 2022;77(1):58–64. doi:10.1136/thoraxjnl-2021-217116. Available from: https://consensus.app/papers/details/0e93a2860bea5c4095cae20274e6f41f/?utm_source
17. Luján M, et al. Evidence on non-invasive respiratory support during flexible bronchoscopy: a narrative review. J Clin Med. 2025;14(18):6658. doi:10.3390/jcm14186658. Available from: https://consensus.app/papers/details/85a65bf968f155df8d1d24a585de63a7/?utm_source
18. Strohleit D, et al. Guidelines on analgesedation, monitoring, and recovery time for flexible bronchoscopy: a systematic review. BMC Pulm Med. 2021. doi:10.1186/s12890-021-01532-4.

- Available from:
https://consensus.app/papers/details/9b59dd4b73015a8c8acd2e9613c15b3d/?utm_source
19. Wang LF, et al. Comparative analysis of guidelines and recommendations for sedation during flexible bronchoscopy: a narrative review. Eur Respir Rev. 2025. doi:10.1183/16000617.0045-2025. Available from:
https://consensus.app/papers/details/80496d667d575146a0ba851c5abedf26/?utm_source
20. Grendelmeier P, et al. Flexible bronchoscopy with moderate sedation in COPD: a case-control study. Int J Chron Obstruct Pulmon Dis. 2017. doi:10.2147/COPD.S119575. Available from:
https://consensus.app/papers/details/1673157e52c25c158513dc1c8b7159ed/?utm_source
21. Kim SY, et al. Association between oxygen saturation level during bronchoscopy and post-bronchoscopy adverse events: a retrospective cohort study. Respir Res. 2022. doi:10.1186/s12931-022-02063-0. Available from:
https://consensus.app/papers/details/1e13f0b6f88f5eacb9756bf3c2c5833e/?utm_source
22. Patolia S, et al. Bronchoscopy in intubated and non-intubated intensive care unit patients with respiratory failure. J Thorac Dis. 2021. doi:10.21037/jtd-19-3709. Available from:
https://consensus.app/papers/details/5496d9e1dd0554ea918b18c231ebb399/?utm_source
23. Nanavaty P, et al. Go with the flow? High flow nasal cannula for bronchoscopy. Thorax. 2021. doi:10.1136/thoraxjnl-2021-217450. Available from:
https://consensus.app/papers/details/dd2e8b9ea5c059fda01c96019b1e7037/?utm_source
24. Delorme M, et al. Physiologic effects of high-flow nasal cannula in healthy subjects. Respir Care. 2020. doi:10.4187/respcare.07306. Available from:
https://consensus.app/papers/details/40b2f1a3318e5605816aab5edbc69681/?utm_source
25. Okuda M, et al. Evaluation by various methods of the physiological mechanism of a high-flow nasal cannula (HFNC) in healthy volunteers. BMJ Open Respir Res. 2017;4(1):e000200. doi:10.1136/bmjresp-2017-000200. Available from:
https://consensus.app/papers/details/49447c69de76568c93a7b9edac47b404/?utm_source
26. Onodera Y, et al. A high-flow nasal cannula system with relatively low flow effectively washes out CO₂ from the anatomical dead space in a sophisticated respiratory model made by a 3D

- printer. Intensive Care Med Exp. 2018. doi:10.1186/s40635-018-0172-7. Available from: https://consensus.app/papers/details/17791851b40f5466a49ae62cd19cd8fe/?utm_source
27. Pinkham M, et al. Effect of respiratory rate and size of cannula on pressure and dead-space clearance during nasal high flow in patients with COPD and acute respiratory failure. J Appl Physiol. 2022. doi:10.1152/japplphysiol.00769.2021. Available from: https://consensus.app/papers/details/5f76de84a69a58d2b3a992653669cfa2/?utm_source
28. Tatkov S, et al. Asymmetrical nasal high flow ventilation improves clearance of CO₂ from the anatomical dead space and increases positive airway pressure. J Appl Physiol. 2023. doi:10.1152/japplphysiol.00692.2022. Available from: https://consensus.app/papers/details/dd0d2f0d422e5869b32986eec3b26d75/?utm_source
29. Su CL, Chiang LL, Tam KW, et al. High-flow nasal cannula for reducing hypoxemic events in patients undergoing bronchoscopy: a systematic review and meta-analysis of randomized trials. PLoS One. 2021;16(12):e0260716. doi:10.1371/journal.pone.0260716. Available from: https://consensus.app/papers/details/cbb3bd793f29576eb5bda568fe86edd6/?utm_source
30. Sampsonas F, Karamouzou V, Karampitsakos T, et al. High-flow vs. low-flow nasal cannula in reducing hypoxemic events during bronchoscopic procedures: a systematic review and meta-analysis. Front Med (Lausanne). 2022;9:815799. doi:10.3389/fmed.2022.815799. Available from: https://consensus.app/papers/details/aeb77e60e7f75a9bbe80b3194543ec44/?utm_source
31. Roy A, Khanna P, Chowdhury SR, Haritha D, Sarkar S. The impact of high-flow nasal cannula vs other oxygen delivery devices during bronchoscopy under sedation: a systematic review and meta-analyses. Indian J Crit Care Med. 2022;26(10):1131–40. doi:10.5005/jp-journals-10071-24339. Available from: https://consensus.app/papers/details/28cee48e1ea256ac8441d082aab8d147/?utm_source
32. Tao Y, Sun M, Miao M, et al. High flow nasal cannula for patients undergoing bronchoscopy and gastrointestinal endoscopy: a systematic review and meta-analysis. Front Surg. 2022;9:949614. doi:10.3389/fsurg.2022.949614. Available from: https://consensus.app/papers/details/74996faf13c85d618c2ab0dc0d447e1d/?utm_source

33. Wei C, et al. The effectiveness of transnasal high flow nasal cannula in bronchoscopy under sedation: a systematic review and meta-analysis. *Front Med (Lausanne)*. 2024;11:1428431. doi:10.3389/fmed.2024.1428431. Available from: https://consensus.app/papers/details/07859a46f6325ba197a619fde54354a2/?utm_source
34. Nishie K, et al. Efficacy of high-flow nasal cannula oxygen therapy during bronchoscopy: a systematic review and meta-analysis. *J Bronchology Interv Pulmonol*. 2026. doi:10.1097/LBR.0000000000001054. Available from: https://consensus.app/papers/details/bb2e86b017825896993cb30e176f8780/?utm_source
35. Fliess de Castro RM, et al. High-flow nasal cannula versus conventional oxygen therapy during bronchoscopy: a meta-analysis of randomized controlled trials. *J Bronchology Interv Pulmonol*. 2026. doi:10.1097/LBR.0000000000001063. Available from: https://consensus.app/papers/details/9a506e7b338e5214910e48c73cf89ae9/?utm_source
36. Sehgal I, et al. An RCT to compare high flow nasal cannula with standard nasal cannula to prevent desaturation in subjects undergoing EBUS-TBNA: HIFLO-EBUS trial. *Lung India*. 2025. doi:10.4103/lungindia.lungindia_128_25. Available from: https://consensus.app/papers/details/7b864e16abe05f30999d7301d6c6a72e/?utm_source
37. Wang M, et al. High-flow nasal cannula oxygenation reduces desaturation risk during diagnostic flexible bronchoscopy under deep sedation: a randomized controlled trial. *Front Med (Lausanne)*. 2026. doi:10.3389/fmed.2025.1729660. Available from: https://consensus.app/papers/details/b1abed6603e95bcba73394faabb77ef0/?utm_source
38. Wang R, Zhao Y, Lan N, Wang W, Tang X, Li T, et al. High-flow nasal oxygen therapy via a single-prong cannula interface during bronchoscopy in patients with acute respiratory failure: a two-center, open-label, randomized controlled trial. *Ann Intensive Care*. 2026;16:100081. doi:10.1016/j.aicoj.2026.100081. Available from: https://consensus.app/papers/details/f5f4816cfa1652788736052bb146eae1/?utm_source
39. Longhini F, et al. Practice of oxygenation and respiratory support during fibreoptic bronchoscopy: the OxyFOB study protocol. *BMJ Open*. 2025. doi:10.1136/bmjopen-2025-104747. Available from: https://consensus.app/papers/details/ac459e9d85215906ba584704e02e25dd/?utm_source

40. Schünemann HJ, et al. GRADE guidelines: 18. How ROBINS-I and other tools to assess risk of bias in non-randomized studies should be used to rate the certainty of a body of evidence. *J Clin Epidemiol.* 2019;111:105–14. doi:10.1016/j.jclinepi.2018.01.012. Available from: https://consensus.app/papers/details/b3cfd8b34b995deb9090d3c9b5eb7a72/?utm_source
41. Yilmazel Ucar E, Araz Ö, Kerget B, Akgun M, Saglam L. Comparison of high-flow and conventional nasal cannula oxygen in patients undergoing endobronchial ultrasonography. *Intern Med J.* 2021;51(11):1935–9. doi:10.1111/imj.15001. Available from: https://consensus.app/papers/details/9841e2c9f3d0557ba273ef9cd9335c34/?utm_source
42. Ben-Menachem E, McKenzie J, O'Sullivan C, Havryk AP. High-flow nasal oxygen versus standard oxygen during flexible bronchoscopy in lung transplant patients: a randomized controlled trial. *J Bronchology Interv Pulmonol.* 2020;27(4):259–65. doi:10.1097/LBR.0000000000000670. Available from: https://consensus.app/papers/details/a06252ef70fb5f15994b19e9f0c63b6f/?utm_source
43. Flemyng E, et al. Using Risk of Bias 2 to assess results from randomised controlled trials: guidance from Cochrane. *BMJ Evid Based Med.* 2023. doi:10.1136/bmjebm-2022-112102. Available from: https://consensus.app/papers/details/46685b6f9d4f58eda2446123df4524cb/?utm_source
44. Lucangelo U, et al. High-flow nasal interface improves oxygenation in patients undergoing bronchoscopy. *Crit Care Res Pract.* 2012;2012:506382. doi:10.1155/2012/506382. Available from: https://consensus.app/papers/details/cbfcebdd4cc35079bac13707a4d2d3d2/?utm_source
45. Irfan M, Ahmed M, Breen D. Assessment of high flow nasal cannula oxygenation in endobronchial ultrasound bronchoscopy: a randomized controlled trial. *J Bronchology Interv Pulmonol.* 2021;28(2):130–7. doi:10.1097/LBR.0000000000000719. Available from: https://consensus.app/papers/details/9b21abf0cbdf540bac633e365ec53cd1/?utm_source
46. Sharluyan A, et al. High flow nasal cannula versus standard low flow nasal oxygen during flexible bronchoscopy in children: a randomized controlled trial. *Pediatr Pulmonol.* 2021. doi:10.1002/ppul.25655. Available from: https://consensus.app/papers/details/eae713b6c3005751b048652cf75aaf76/?utm_source

47. Zhang W, Wang JL, Fu S, Zhou JM, Zhu YJ, Cai SN, et al. Incidence of oxygen desaturation using a high-flow nasal cannula versus a facemask during flexible bronchoscopy in patients at risk of hypoxemia: a randomised controlled trial. *BMC Pulm Med.* 2022;22(1). doi:10.1186/s12890-022-02188-4. Available from: https://consensus.app/papers/details/6a0172ee384650fdbd1fa85bce6406af/?utm_source
48. Freund O, et al. Laryngeal mask airway or high-flow nasal cannula versus nasal cannula for advanced bronchoscopy: a randomised controlled trial. *ERJ Open Res.* 2024. doi:10.1183/23120541.00421-2024. Available from: https://consensus.app/papers/details/3069f706ab0453a99d34267fd6f4428e/?utm_source
49. Kim HJ, et al. Comparison of high-flow nasal oxygenation and standard low-flow nasal oxygenation during rigid bronchoscopy: a randomized controlled trial. *Korean J Anesthesiol.* 2024. doi:10.4097/kja.24517. Available from: https://consensus.app/papers/details/eae3c4ffd90b5c099b715626877eed20/?utm_source
50. Gupta S, et al. Effect of high flow nasal cannula versus conventional nasal cannula oxygen therapy in patients undergoing endobronchial ultrasound-guided transbronchial needle aspiration. *Monaldi Arch Chest Dis.* 2025. doi:10.4081/monaldi.2025.3246. Available from: https://consensus.app/papers/details/da45deefaef556da813190f5ba41f460/?utm_source
51. Yue F, et al. Clinical observations of high-flow nasal cannula oxygenation in endobronchial ultrasound-guided transbronchial needle aspiration: a randomized controlled study. *Front Med (Lausanne).* 2025;12:1634020. doi:10.3389/fmed.2025.1634020. Available from: https://consensus.app/papers/details/f8e47d77b7d85ee292dcf939342530da/?utm_source
52. Takakuwa O, Oguri T, Asano T, et al. Prevention of hypoxemia during endobronchial ultrasound-guided transbronchial needle aspiration: usefulness of high-flow nasal cannula. *Respir Investig.* 2018;56:418–23. doi:10.1016/j.resinv.2018.06.004. Available from: https://consensus.app/papers/details/0c57d5667f375620bc1dfb08ad3902b2/?utm_source
53. Kim EJ, Jung CY, Kim KC. Effectiveness and safety of high-flow nasal cannula oxygen delivery during bronchoalveolar lavage in acute respiratory failure patients. *Tuberc Respir Dis (Seoul).*

- 2018;81(4):319–29. doi:10.4046/trd.2017.0122. Available from:
https://consensus.app/papers/details/0ee4696635535a4ab142af496fb9f400/?utm_source
54. Chung S, et al. Clinical effectiveness of high-flow nasal cannula in hypoxaemic patients during bronchoscopic procedures. *Tuberc Respir Dis (Seoul)*. 2018. doi:10.4046/trd.2017.0104. Available from:
https://consensus.app/papers/details/872bfa6033be5cb3ad02e58bffd8dfc0/?utm_source
55. Service J, et al. Prospective experience of high-flow nasal oxygen during bronchoscopy in 182 patients: a feasibility study. *J Bronchology Interv Pulmonol*. 2019. doi:10.1097/LBR.0000000000000533. Available from:
https://consensus.app/papers/details/bb4f00af20195b51a2d0828c2c75602c/?utm_source
56. Nilushi PSMT, et al. Evaluation of patient outcomes of high flow versus low flow nasal oxygen during outpatient bronchoscopy under conscious sedation at Thoracic Procedure Suite in Lyell McEwin Hospital. *Int J Respir Pulm Med*. 2022. doi:10.23937/2378-3516/1410169. Available from: https://consensus.app/papers/details/530cde7c29d15061a07ecad789a13d38/?utm_source
57. Arias-Sánchez P, et al. Changes in oxygen saturation during fiberoptic bronchoscopy: high-flow nasal cannula versus standard oxygen therapy. *Respir Care*. 2023. doi:10.4187/respcare.10598. Available from:
https://consensus.app/papers/details/09a471b33f2d53aaaadeaa22df2fd3e9/?utm_source
58. Ravi P, et al. Is high-flow nasal oxygenation a game changer in endobronchial ultrasound-guided transbronchial needle aspiration? *Sultan Qaboos Univ Med J*. 2023. doi:10.18295/squmj.12.2023.086. Available from:
https://consensus.app/papers/details/371024e7e5a75823ab2be575f9577198/?utm_source
59. Luo X, et al. High-flow nasal cannula oxygen therapy versus conventional oxygen therapy in patients undergoing bronchoscopy: a retrospective study. *BMC Pulm Med*. 2024. doi:10.1186/s12890-024-03440-9. Available from:
https://consensus.app/papers/details/084651e75adc5706a8385ae58344ead2/?utm_source
60. de Vico P, et al. Evaluation of high flow nasal cannulae during endobronchial ultrasound bronchoscopy (EBUS) in high anaesthetic risk patients: a monocentric prospective study. *BMC*

- Anesthesiol. 2025. doi:10.1186/s12871-025-03447-7. Available from:
https://consensus.app/papers/details/ad3e3da7383958b38d3ba11012786ee8/?utm_source
61. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol. 2014;14:135. doi:10.1186/1471-2288-14-135. Available from:
https://consensus.app/papers/details/8123cbd49f0a5a5795aa835a99387201/?utm_source
62. Sterne JAC, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. BMJ. 2011;343:d4002. doi:10.1136/bmj.d4002. Available from:
https://consensus.app/papers/details/37fc12e758405694a8068a87d7f3a59d/?utm_source
63. Wang J, et al. High flow nasal cannula versus conventional oxygen therapy during bronchoscopy: a systematic review and individual participant data meta-analysis. Pulmonology. 2026. doi:10.1080/25310429.2026.2613485. Available from:
https://consensus.app/papers/details/4322fedba7d855959718df6f526c0f77/?utm_source
64. Liu H, et al. High-flow nasal cannula oxygen therapy: physiological basis and clinical applications in anesthesia. Front Med (Lausanne). 2025. doi:10.3389/fmed.2025.1661569. Available from:
https://consensus.app/papers/details/6715025ab32c5591b60d49be6a0a20e4/?utm_source
65. Spicuzza L, et al. High-flow nasal cannula oxygen therapy as an emerging option for respiratory failure: the present and the future. Ther Adv Chronic Dis. 2020. doi:10.1177/2040622320920106. Available from:
https://consensus.app/papers/details/2fdaeec31d89515599e9d2065479d184/?utm_source
66. Thiruvengkatarajan V, et al. Effect of high-flow nasal oxygen on hypoxaemia during procedural sedation: a systematic review and meta-analysis. Anaesthesia. 2022. doi:10.1111/anae.15845. Available from:
https://consensus.app/papers/details/4b534688ae6c5470bcdf7f2e36d32ba2/?utm_source
67. Wang W, et al. Efficacy of high-flow nasal cannula versus conventional oxygen therapy in high-risk patients undergoing bronchoscopy: a meta-analysis of RCTs. Respir Med. 2026.

- doi:10.1016/j.rmed.2026.108664. Available from:
https://consensus.app/papers/details/becdad7fbd17590881a73aa8bceb087b/?utm_source
68. Wang LL, et al. Effect of high flow nasal cannula oxygenation on incidence of hypoxia during sedated gastrointestinal endoscopy in patients with obesity: multicentre randomised controlled trial. BMJ. 2025. doi:10.1136/bmj-2024-080795. Available from:
https://consensus.app/papers/details/1ebc0e3cac8452f8b04de7e6df4c69ac/?utm_source
69. Hung KC, et al. Efficacy of high-flow nasal oxygenation against peri- and post-procedural hypoxemia in patients with obesity: a meta-analysis of randomized controlled trials. Sci Rep. 2022. doi:10.1038/s41598-022-10396-5. Available from:
https://consensus.app/papers/details/620a8e59258750b9923c73fc335ab2d0/?utm_source
70. Zhou R, et al. Efficacy of high-flow nasal cannula versus conventional oxygen therapy in obese patients during the perioperative period: a systematic review and meta-analysis. Can Respir J. 2022. doi:10.1155/2022/4415313. Available from:
https://consensus.app/papers/details/9a83053f4a6c5870884e4a1b6f5309c4/?utm_source