

SYSTEMATIC REVIEW / META-ANALYSIS

Conservative versus Liberal Oxygenation Targets in Acutely Ill Children Across the Continuum of Care: A Systematic Review and Meta-Analysis of Randomised Controlled Trials

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ARTICLE INFO	ABSTRACT
ARTICLE TYPE Systematic Review / Meta-Analysis ARTICLE HISTORY Received: July 30, 2026 Revised: August 25, 2026 Accepted: September 24, 2026 Available online: September 28, 2026 Published: September 30, 2026 KEYWORDS Child; Hyperoxia; Infant; Intensive care units, paediatric; Oximetry; Oxygen inhalation therapy CORRESPONDING AUTHOR Ahmad Iqbal Romdloni E-mail: iqbalromdloni@gmail.com DOI https://doi.org/10.59345/sjped.v4i2.347 LICENSE CC BY-NC-SA 4.0 COPYRIGHT © 2026 The Author(s). Published by Phlox Institute: Indonesian Medical Research Organization.	Background: Supplemental oxygen is common in paediatric care, but target saturation is not standardised and excessive exposure has been associated with organ dysfunction and death. Objective: To compare conservative and liberal oxygenation targets for mortality, serious adverse events, length of stay, and treatment failure in acutely ill children. Methods: PubMed/MEDLINE, trial registers, and citation networks were searched to July 15, 2026 for randomised trials of lower versus higher oxygen saturation targets in children aged over 38 weeks corrected gestational age to 18 years. Risk of bias was assessed with RoB 2, certainty with GRADE, and outcomes with random-effects models. Results: Ten trials involving 5,171 children were included. Death occurred in 69/2,114 children managed conservatively and 71/2,121 managed liberally (risk ratio 0.99, 95% CI 0.72 to 1.37; risk difference -0.4 percentage points, 95% CI -1.2 to 0.4). Serious adverse events were similar (risk ratio 0.86, 95% CI 0.65 to 1.14). Hospital stay was shorter with conservative targets (standardised mean difference -0.28, 95% CI -0.52 to -0.04), with benefit confined to ward and emergency settings. Intensive care stay showed no clear difference. Treatment failure was more frequent with conservative care (risk ratio 2.63, 95% CI 1.43 to 4.84) without excess deaths. Conclusion: Conservative targets did not increase mortality or serious adverse events and shortened hospital stay outside intensive care. Their higher treatment-failure rate supports use only with close monitoring and prompt escalation.

1. Introduction

Supplemental oxygen remained one of the most frequently administered treatments in paediatric acute care, and hypoxaemia remained one of the strongest single predictors of death in children with acute respiratory illness. Among children hospitalised with World Health Organization-defined severe pneumonia in Bangladesh, 40% were hypoxaemic on admission and hypoxaemia carried an adjusted odds ratio for in-hospital death of 11.08 (95% CI 7.28 to 16.87).¹ A cohort of 7,196 Indian children under five years of age with severe community-acquired pneumonia reported hypoxic pneumonia in 35.9% and an adjusted odds ratio for death of 2.36 (95% CI 1.42 to 3.92).² and a meta-analysis of 33 studies comprising 155,633 children with lower respiratory infection in low-income and middle-income countries found that a peripheral oxygen saturation measured by pulse oximetry (SpO₂) below 90% was associated with an odds ratio for death of 4.75 (95% CI 3.42 to 6.58).³ Risk was not confined to profound hypoxaemia: in 3,848 Bangladeshi infants with suspected pneumonia, an SpO₂ of 90–93% carried an adjusted risk ratio for death of 4.3 relative to an SpO₂ of 94–100%.⁴ The clinical reflex to correct a low saturation therefore developed for good reason.

The corollary received far less attention. Oxygen is a drug with a dose, and the upper end of that dose has been associated with harm. In 5,406 mechanically ventilated children, the highest quartile of cumulative excess oxygen exposure during

the first day of ventilation was associated with multiple organ dysfunction and death.⁵ An analysis of 4,003 paediatric critical care admissions and 75,129 blood gases found excess mortality after any extreme hyperoxaemic event, rising with the number of such events, and treatment that produced an SpO₂ above 98% was the commonest antecedent.⁶ Admission arterial oxygen tension showed a U-shaped relationship with mortality across 13,071 paediatric intensive care encounters, with the highest mortality at both extremes.⁷ Comparable associations were reported after paediatric cardiac arrest,⁸ during extracorporeal membrane oxygenation⁹ and on cardiopulmonary bypass, where hyperoxia was independently associated with operative mortality (odds ratio 4.3, 95% CI 1.4 to 13.2).^{10,11} Experimental work supplied a plausible mechanism: hyperoxia generated reactive oxygen species, drove NOX4-dependent alveolar epithelial apoptosis,¹² triggered ferroptosis and impaired alveolarisation in newborn mice,¹³ induced senescence in human fetal airway smooth muscle,¹⁴ and produced lasting cerebrovascular and neurocognitive deficits in exposed animals.¹⁵ Children randomised to a liberal oxygenation target in the pilot Oxy-PICU trial excreted more urinary nitrate and nitrite than those randomised to a conservative target, indicating that the same oxidative pathways were engaged at the bedside.¹⁶

Adult intensive care answered this question first, and answered it ambiguously. A lower arterial oxygen target did not reduce 90-day mortality in patients with acute hypoxaemic respiratory failure (adjusted risk ratio 1.02, 95% CI 0.94 to

1.11),¹⁷ ventilator-free days were identical across three saturation targets in 2,541 ventilated adults,¹⁸ and conservative oxygen therapy in 16,500 adults reduced oxygen exposure by 29% without changing 90-day mortality.¹⁹ Restrictive targets were also neutral after cardiac arrest,^{20,21} whereas a lower target increased days alive without life support in critically ill adults with COVID-19.^{22,23} An individual patient data meta-analysis of 3,585 adults found a pooled risk ratio for death of 0.99 (95% CI 0.92 to 1.07) with signals of subgroup heterogeneity,²⁴ and machine-learning analysis of two trials suggested that individual treatment effects ranged from a 27.2% absolute reduction to a 34.4% absolute increase in mortality.²⁵ Adults, however, are not a reliable model for children, whose oxygen consumption per kilogram, haemoglobin-oxygen affinity, functional residual capacity and cardiovascular reserve differ, and whose acute illness is dominated by airway and parenchymal respiratory disease rather than by cardiac and septic pathology.

Paediatric evidence accumulated slowly, in fragments, and in very different settings. Trials have compared saturation targets in mechanically ventilated children in intensive care, oxygen-initiation thresholds on general wards in high-income systems, permissive hypoxaemia in African district hospitals where oxygen is scarce, and titrated versus high-concentration oxygen in emergency departments. These settings differ in monitoring intensity, in the ability to escalate care and in background mortality, yet they share a single physiological question. The most recent qualitative synthesis of paediatric saturation targets pre-dated the definitive Oxy-PICU trial and the trials reported in 2025 and 2026, and did not pool outcomes quantitatively.²⁶ Practice, meanwhile, remained inconsistent: pulse oximetry was used in fewer than half of paediatric admissions across Kenyan hospitals over seven years,²⁷ only 24% of primary facilities in a seven-country survey had a functional pulse oximeter,²⁸ and oxygen supply remains a rationed resource in many systems where paediatric pneumonia is most common.^{29–32}

The novelty of this study lies in being the first quantitative synthesis to pool every randomised comparison of conservative and liberal oxygenation targets across the whole continuum of paediatric acute care — intensive care, ward and emergency department — including two trials published in 2025 and 2026 that have not previously been meta-analysed, and in testing whether the effect of a lower target differed between settings that differ fundamentally in their capacity to detect and reverse deterioration. The aim of this study was to determine whether conservative oxygenation targets, compared with liberal targets, altered all-cause mortality, serious adverse events, hospital and intensive care length of stay, and treatment failure in acutely ill children beyond the neonatal period.

2. Methods

Study design

This systematic review and meta-analysis was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. The review synthesised aggregate data from published randomised controlled trials; no individual patient data were obtained and no new human or animal data were generated, so institutional review board approval and informed consent were not applicable.

Search strategy

PubMed/MEDLINE was searched natively from inception to July 15, 2026 using fourteen Boolean strings that combined Medical Subject Headings with free-text terms, supplemented by searches of ClinicalTrials.gov and the ISRCTN registry, by forward-citation tracking of the index trials in Europe PMC, by backward-citation screening of the reference list of the most recent qualitative synthesis,²⁶ and by free-text searching of the Directory of Open Access Journals and Google Scholar. The core string was: ("oxygen saturation target" OR "oxygenation target" OR "oxygen threshold" OR "conservative oxygen" OR "liberal oxygen" OR "permissive hypox" OR "titrated oxygen") AND (child OR infant OR paediatric OR pediatric OR bronchiolitis OR PICU OR "Child"[Mesh] OR "Infant"[Mesh]) AND (randomised controlled trial[pt] OR randomi*[tiab] OR "controlled clinical trial"[pt]). Searches were restricted to reports published in English; no date restriction was applied. The full set of strings, databases and hit counts is reproduced in the supplementary search record. Records from the Cochrane Central Register of Controlled Trials were identified through PubMed-indexed trial records and register cross-checking rather than through a native CENTRAL interface, and Embase was not searched; both are acknowledged as limitations of the search.

Eligibility criteria

Eligibility followed a PICOS framework, as detailed in Table 1. Trials were included when they randomised children older than 38 weeks corrected gestational age and younger than 18 years who were acutely ill in a paediatric intensive care unit, a paediatric ward or an emergency department, to a lower versus a higher SpO₂ target or oxygen-administration threshold. Display-modified oximetry was accepted as a conservative intervention because it lowers the effective threshold at which oxygen is given while preserving blinding. Trials confined to neonatal intensive care or to preterm-specific conditions were excluded, as were trials of intra-operative cardiopulmonary bypass oxygenation, of automated versus manual titration to the same target, and of monitoring modality rather than target.

Table 1. Eligibility criteria for the review.

Element	Inclusion	Exclusion
Population	Children >38 weeks corrected gestational age to <18 years with acute illness in a paediatric intensive care unit, paediatric ward or emergency department	Neonatal intensive care; preterm-specific conditions; cyanotic congenital heart disease; pulmonary hypertension; chronic lung disease requiring long-term oxygen
Intervention	Conservative oxygenation: lower SpO ₂ target or oxygen-initiation threshold, down-titrated oxygen, oxygen withheld within a defined saturation band, or display-modified oximetry lowering the effective threshold	Intra-operative cardiopulmonary bypass oxygenation; automated versus manual titration to the same target; monitoring modality alone
Comparator	Liberal oxygenation: higher or conventional SpO ₂ target or threshold, or high-concentration oxygen	No comparison group; comparison of oxygen delivery device alone
Outcomes	All-cause mortality (primary); serious adverse events; hospital and intensive care length of stay; treatment failure; hospital admission	Physiological endpoints reported without any clinical outcome
Study design	Randomised controlled trials, including pilot and feasibility trials, published in English in peer-reviewed indexed journals	Non-randomised studies; reviews; editorials; protocols; conference abstracts

Study selection and data extraction

Records were de-duplicated and screened by title and abstract, and potentially eligible reports were assessed in full text against the criteria above, with disagreements resolved by discussion. For every included trial the following were extracted: citation and digital object identifier, country, setting, design, eligibility criteria, the definition of each oxygenation arm, numbers randomised and analysed, age and sex, follow-up duration, and all outcome data. Every digital object identifier was verified against the PubMed record and Crossref before the trial was included. Values that were not reported were recorded as such and were never imputed; where a published percentage could not be resolved into an exact numerator, the outcome was excluded from pooling rather than back-calculated.

Medians with interquartile ranges were converted to means with standard deviations using the method of Wan and colleagues, an approach whose accuracy for skewed outcomes has been confirmed in recent simulation work;³³ every converted value was flagged, and a sensitivity analysis restricted to trials reporting means and standard deviations directly was pre-specified. In the two trials with three randomised arms, the two liberal arms were combined using the standard formulae for pooling group means and standard deviations, so that no child contributed twice.

Two reviewers screened records, extracted data and assessed risk of bias independently, and disagreements were resolved by discussion with a third reviewer; formal agreement statistics were not calculated. Authors of trials with irrecoverable numerators were not contacted, so those outcomes remained unpooled.

Outcomes

The primary outcome was all-cause mortality at the latest timepoint reported up to 30 days. Secondary outcomes were serious adverse events, defined as the number of children experiencing at least one such event; hospital length of stay; length of stay in the paediatric intensive care unit; and, as an exploratory safety outcome, treatment failure as defined by each trial. Hospital admission was examined separately in the emergency-department trials.

Risk of bias assessment

Risk of bias was assessed with the Cochrane risk-of-bias 2 tool across the five domains of the randomisation process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result, each judged as low risk, some concerns or high risk, with an overall judgement derived by the tool's algorithm.

Statistical analysis

Analyses were performed in R version 4.5.3 with the meta (version 8.2.1) and metafor (version 4.8.0) packages, and all analyses followed the intention-to-treat populations reported by the trials. Dichotomous outcomes were pooled as risk ratios using the Mantel-Haenszel method without

continuity correction for trials with a zero cell, and risk differences were calculated in parallel because they remain estimable when events are rare. Continuous outcomes measured on different scales were pooled as standardised mean differences (Hedges g) and those measured in days as mean differences. Random-effects models with the Paule-Mandel estimator of between-study variance were used for all analyses, because the trials differed in setting, in the saturation bands compared and in illness severity; common-effect estimates are reported alongside as a sensitivity analysis. Heterogeneity was quantified by Cochran Q , tau-squared and I^2 with its confidence interval, and a prediction interval was calculated for the primary outcome. Given the small number of trials, the limitations of random-effects inference with few studies were taken into account when interpreting confidence intervals.³⁴

Pre-specified subgroup analysis compared intensive care with ward and emergency settings, tested by the between-subgroup Q statistic. Robustness was examined by leave-one-out analysis, by refitting the primary outcome as a Peto odds ratio and with a 0.5 continuity correction applied to all trials, and by restricting the length-of-stay analysis to directly reported means. Small-study effects were to be assessed by funnel plot and Egger's test only if at least ten trials contributed to an outcome; because no outcome reached that threshold, the funnel plot is presented for visual inspection alone. A two-sided p value below 0.05 was considered statistically significant.

Mortality was additionally analysed with the timepoint restricted to 28 or 30 days, excluding the trial that used display-modified oximetry, excluding the permissive-hypoxaemia trial, and restricted to trials published from 2021 onwards. Hospital length of stay was re-analysed as a ratio of means, which accommodates the skewed distribution of stay data without standardisation, and with the same three exclusions. Random-effects meta-regression was used to examine whether the treatment effect varied with the control-arm event risk and with the intensive care setting. The certainty of evidence for each outcome was rated with the GRADE approach, with imprecision judged against the prediction interval as well as the confidence interval.^{35,36}

3. Results

Study selection

The searches retrieved 1,413 records from databases and 456 from registers, citation tracking and other sources. After 452 duplicates were removed, 1,417 records were screened by title and abstract and 28 reports were assessed in full text, of which 18 were excluded, most commonly because the intervention was an intra-operative cardiopulmonary bypass oxygenation strategy ($n = 6$) or automated rather than manual titration to an identical target ($n = 5$). Ten randomised controlled trials met all eligibility criteria, as illustrated in Figure 1.^{37–46}

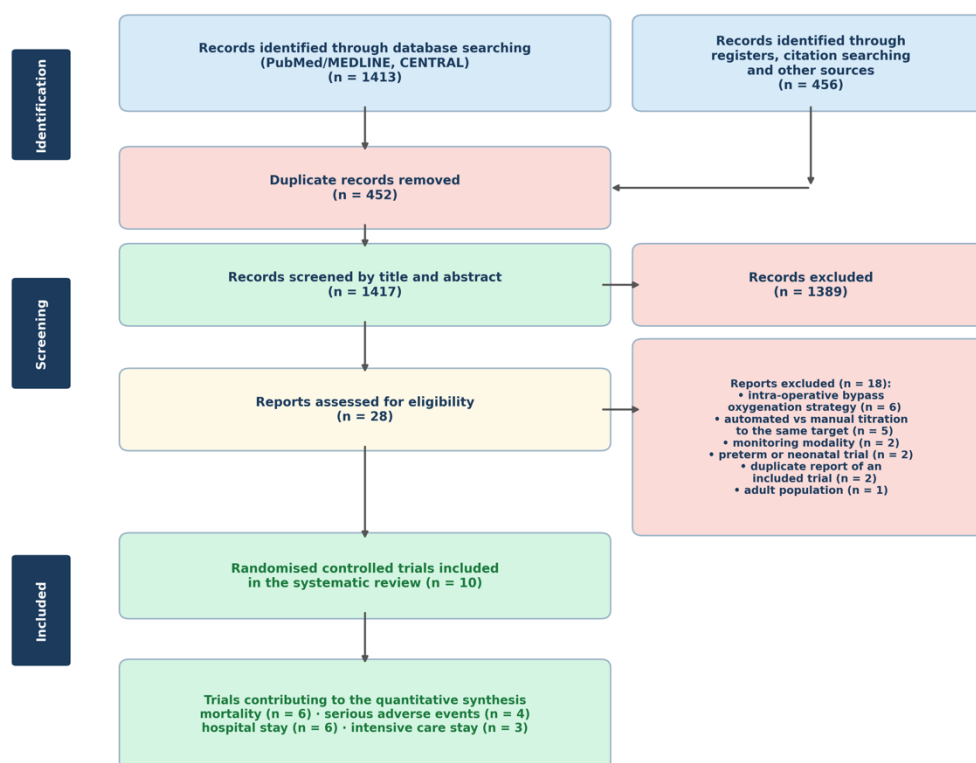


Figure 1. Flow of records through the review, following the PRISMA 2020 statement.

Characteristics of the included trials

The ten trials enrolled 5,171 children between 2008 and 2026 and were conducted in the United Kingdom, the Netherlands, Canada, the United States, India, Malawi, Uganda and Kenya, as detailed in Table 2. Three trials were performed in paediatric intensive care units, five on paediatric wards and two in emergency departments. Populations ranged from infants with bronchiolitis to children with World Health Organization-defined severe pneumonia and to mechanically ventilated children with any acute illness. Conservative interventions comprised an SpO₂ target of 88–92% during respiratory support, oxygen-initiation thresholds of 88%, 90% or 90–93%, display-modified oximetry that lowered the effective threshold by three percentage points, titrated oxygen given only below 92% during nebulisation, and permissive hypoxaemia in which oxygen was withheld until saturation fell below 80%. Comparators were targets above 94%, thresholds

of 92% or 94%, conventional targets of 94–99%, or high-concentration oxygen. Follow-up ranged from the duration of the emergency department visit to one year. Separation between arms was confirmed wherever it was measured: mean saturation differed by 2.7 percentage points and inspired oxygen fraction by 0.08 in the pilot intensive care trial,³⁷ median duration of oxygen therapy fell from 100 to 8 hours in the Indian trial,³⁹ and oxygen was administered to 56% rather than 73% of infants in the bronchiolitis trial.⁴⁰

Nine trials contributed to at least one meta-analysis. The randomised pilot trial of room air versus routine oxygen in normoxaemic severe pneumonia reported no outcome by randomised arm and therefore entered the qualitative synthesis only,⁴⁶ and the asthma trial reported hospitalisation solely as percentages, which could not be resolved into exact numerators and were therefore not pooled.⁴⁵

Table 2. Characteristics of the ten included randomised controlled trials.

Trial	Country	Setting	Design	N	n conservative / liberal	Conservative target	Liberal comparator	Follow-up	Risk of bias
Peters 2018	United Kingdom	PICU	Pilot RCT (open-label)	107	54 / 53	SpO ₂ target 88–92% during invasive or non-invasive respiratory support	SpO ₂ target >94% (usual care)	PICU stay	Some concerns
Peters 2024	United Kingdom	PICU (15 units)	Multicentre RCT (open-label)	1872	939 / 933	SpO ₂ target 88–92% during invasive mechanical ventilation	SpO ₂ target >94% (usual care)	30 days (survival to 1 year)	Low
Verma 2026	India	PICU	RCT (open-label, single centre)	178	89 / 89	SpO ₂ target 88–92% with FiO ₂ titration	Conventional SpO ₂ target 94–99%	30 days	Some concerns
Cunningham 2015	United Kingdom	Paediatric ward	Double-blind RCT (equivalence)	615	307 / 308	Modified oximeter: oxygen given below a true SpO ₂ of 90%	Standard oximeter: oxygen given below SpO ₂ 94%	28 days	Low
Louman 2026	Netherlands	Paediatric ward (10 hospitals)	Multicentre RCT (open-label)	557	278 / 279	Oxygen started/stopped at an SpO ₂ threshold of 88%	Oxygen started/stopped at an SpO ₂ threshold of 92%	90 days	Some concerns
Maitland 2021	Uganda and Kenya	District and referral hospital wards	Multicentre RCT (open-label, fractional factorial)	1454	727 / 727	Permissive hypoxaemia: no immediate oxygen at SpO ₂ 80–91%; oxygen only if SpO ₂ <80%	Liberal oxygenation: immediate low-flow oxygen or high-flow nasal therapy, weaned above SpO ₂ 92%	28 days (90-day neurocognitive)	Some concerns
Joseph 2026	Malawi	District hospital paediatric ward	Pilot RCT (open-label, three arms)	21	7 / 14	Standard WHO care: no supplemental oxygen while SpO ₂ 90–93%	Immediate oxygen titrated to SpO ₂ >=94% (low-flow or high-flow nasal cannula, combined)	14 days	Some concerns
Schuh 2014	Canada	Paediatric emergency department	Double-blind RCT	213	105 / 108	Oximeter displaying SpO ₂ three percentage points above the true value (lower effective oxygen threshold)	Oximeter displaying true SpO ₂ values	72 h	Low

Trial	Country	Setting	Design	N	n conservative / liberal	Conservative target	Liberal comparator	Follow-up	Risk of bias
Patel 2019	United States	Paediatric emergency department	RCT (open-label)	96	47 / 49	Titrate oxygen during nebulisation, given only if SpO ₂ <92%	High-concentration oxygen (100% at 4 L/min) driving every nebulisation	Emergency department stay	Some concerns
Singhi 2012	India	Paediatric ward	Randomised pilot trial	58	29 / 29	Room air with continuous monitoring in normoxaemic severe pneumonia (SpO ₂ >90%)	Routine supplemental oxygen 1–2 L/min despite normoxaemia	Hospital stay	High

Values are as reported in each trial. SpO₂, peripheral oxygen saturation measured by pulse oximetry. The overall risk-of-bias judgement was driven by deviations from intended interventions in the eight open-label trials, and by the absence of an accessible prospective registration in the two trials rated high risk or some concerns for selective reporting.

Risk of bias

Three trials were judged to be at low risk of bias overall, six raised some concerns and one was at high risk, as illustrated in Figure 2. The randomisation process was adequate in eight trials. Deviations from intended interventions were the commonest source of concern, since eight trials were necessarily open-label; the two double-blind trials achieved masking by using modified oximeters.^{40,44} Missing outcome data were rarely problematic, although the

pilot intensive care trial could not obtain consent in 12 of 119 randomised children³⁷ and the Dutch trial did not analyse 9 of 566.⁴¹ Measurement of the outcome was at low risk for mortality in every trial because vital status is objective. Selective reporting was a concern only in the two oldest or smallest trials, which lacked accessible prospective registration.^{45,46}

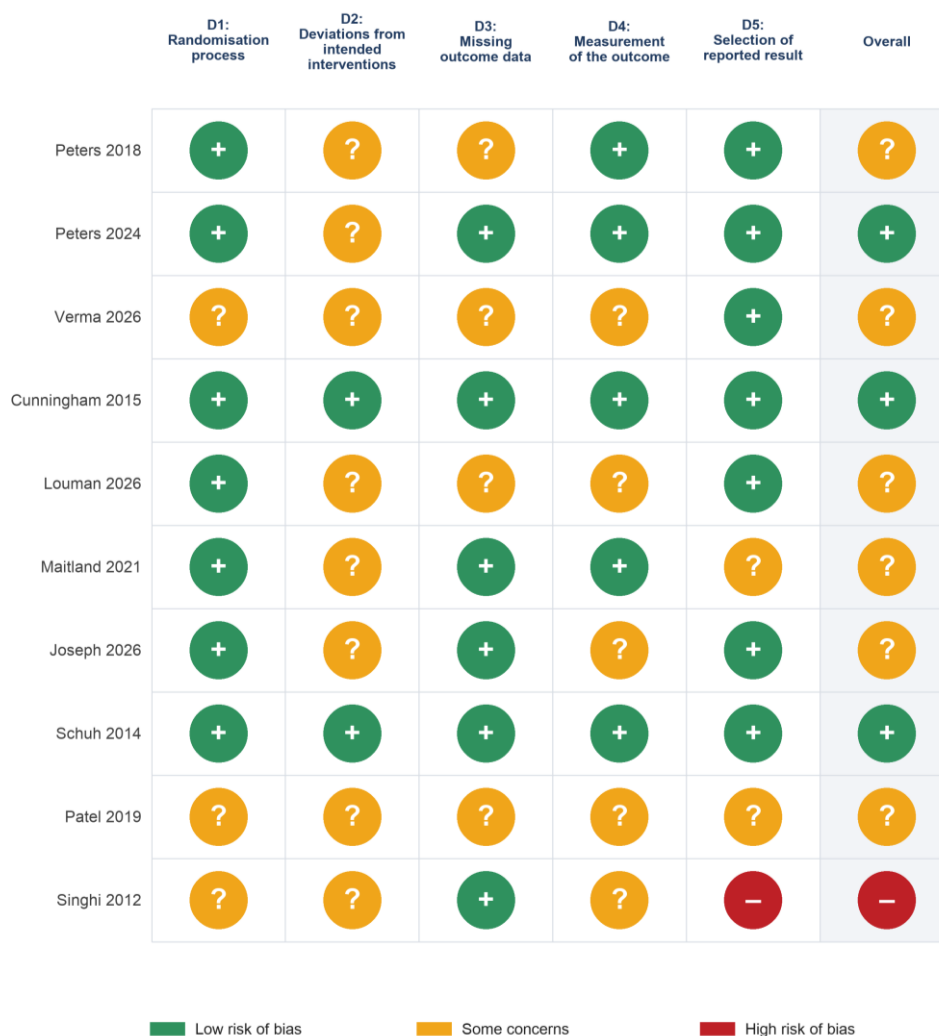


Figure 2. Risk-of-bias assessment of the ten included trials using the Cochrane risk-of-bias 2 tool. Green with a plus sign denotes low risk, amber with a question mark some concerns, and red with a minus sign high risk.

All-cause mortality

Six trials reported mortality by randomised arm and contributed 4,235 children and 140 deaths (69 with conservative targets and 71 with liberal targets). The pooled risk ratio was 0.99 (95% CI 0.72 to 1.37), $p = 0.96$, with no detectable heterogeneity ($I^2 = 0\%$, tau-squared = 0, $Q = 3.34$, $df = 5$, $p = 0.65$), as illustrated in Figure 3. The corresponding risk difference was –0.4 percentage points (95% CI –1.2 to 0.4), and the 95% prediction interval extended from 0.65 to 1.52.

No individual trial showed a significant difference. Estimates ranged from 0.20 in the bronchiolitis trial, in which no death occurred in the conservative arm and two occurred in the liberal arm,⁴⁰ to 5.80 in the 21-child Malawian pilot trial, whose single death gave an interval spanning two orders of magnitude.⁴³ The two trials carrying most weight were the definitive intensive care trial (risk ratio 0.82, 95% CI 0.47 to 1.41; weight 35.3%)³⁸ and the African pneumonia trial (risk ratio 1.05, 95% CI 0.62 to 1.76; weight 38.9%),⁴² which pointed

in opposite directions without reaching significance. Trial-level data are presented in Table 3.

Mortality did not differ between care settings: the risk ratio was 0.96 (95% CI 0.63 to 1.46) across the three intensive

care trials ($I^2 = 0.0\%$) and 1.05 (95% CI 0.33 to 3.36) across the three ward or emergency trials ($I^2 = 14.1\%$), with a test for subgroup differences of $Q = 0.02$, $df = 1$, $p = 0.88$, as detailed in Table 4.

Table 3. Trial-level data for all-cause mortality and the pooled estimate.

Trial	Setting	Timepoint	Deaths / n, conservative	Deaths / n, liberal	Risk ratio (95% CI)	Weight
Peters 2018	Intensive care	PICU discharge	4/54	4/53	0.98 (0.26 to 3.72)	5.9%
Peters 2024	Intensive care	30 days	23/939	28/933	0.82 (0.47 to 1.41)	35.3%
Verma 2026	Intensive care	30 days	13/89	10/89	1.30 (0.60 to 2.81)	17.6%
Cunningham 2015	Ward or emergency department	28 days	0/307	2/308	0.20 (0.01 to 4.16)	1.1%
Maitland 2021	Ward or emergency department	28 days	28/718	27/724	1.05 (0.62 to 1.76)	38.9%
Joseph 2026	Ward or emergency department	14 days	1/7	0/14	5.80 (0.27 to 125.80)	1.1%
Pooled (random effects)	All settings	Latest up to 30 days	69/2,114	71/2,121	0.99 (0.72 to 1.37)	100.0%

All analyses were by intention to treat as reported in each trial.

Table 4. Outcomes by care setting.

Outcome	Setting	Trials	Estimate (95% CI)	I^2	p for subgroup difference
All-cause mortality (risk ratio)	Intensive care	3	0.96 (0.63 to 1.46)	0.0%	0.88
All-cause mortality (risk ratio)	Ward or emergency department	3	1.05 (0.33 to 3.36)	14.1%	0.88
Serious adverse events (risk ratio)	Intensive care	2	0.65 (0.32 to 1.33)	0.0%	0.41
Serious adverse events (risk ratio)	Ward or emergency department	2	0.91 (0.67 to 1.22)	0.0%	0.41
Hospital length of stay (standardised mean difference)	Intensive care	2	-0.06 (-0.20 to 0.07)	23.9%	0.09
Hospital length of stay (standardised mean difference)	Ward or emergency department	4	-0.40 (-0.75 to -0.04)	88.2%	0.09

The p value for subgroup difference applies to the comparison of the two settings within each outcome and is therefore repeated on both rows of that outcome. With three trials per subgroup these comparisons are hypothesis-generating.

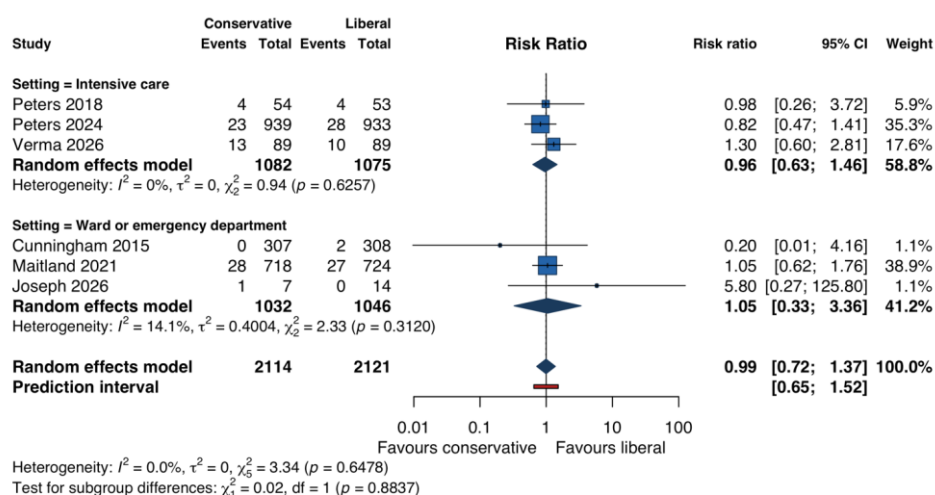


Figure 3. All-cause mortality with conservative versus liberal oxygenation targets, subgrouped by care setting. Squares are proportional to trial weight and the diamond is the random-effects pooled estimate.

Serious adverse events

Four trials reported the number of children with at least one serious adverse event (88 of 2027 with conservative targets and 103 of 2021 with liberal targets). The pooled risk ratio was 0.86 (95% CI 0.65 to 1.14), $p = 0.29$, with no heterogeneity ($I^2 = 0.0\%$), and the pooled risk difference was -0.7 percentage points (95% CI -1.6 to 0.3), as illustrated in Figure 4. Estimates were 0.65 (95% CI 0.32 to 1.33) in intensive care and 0.91 (95% CI 0.67 to 1.22) on wards, with

no subgroup difference ($p = 0.41$). Both prespecified serious adverse events in the pilot intensive care trial were cardiac arrests, and both occurred in the liberal arm.³⁷ In the largest trial, 12 of 939 children managed conservatively and 17 of 933 managed liberally experienced a serious adverse event, and the corresponding totals for any adverse event were 24 and 36.³⁸

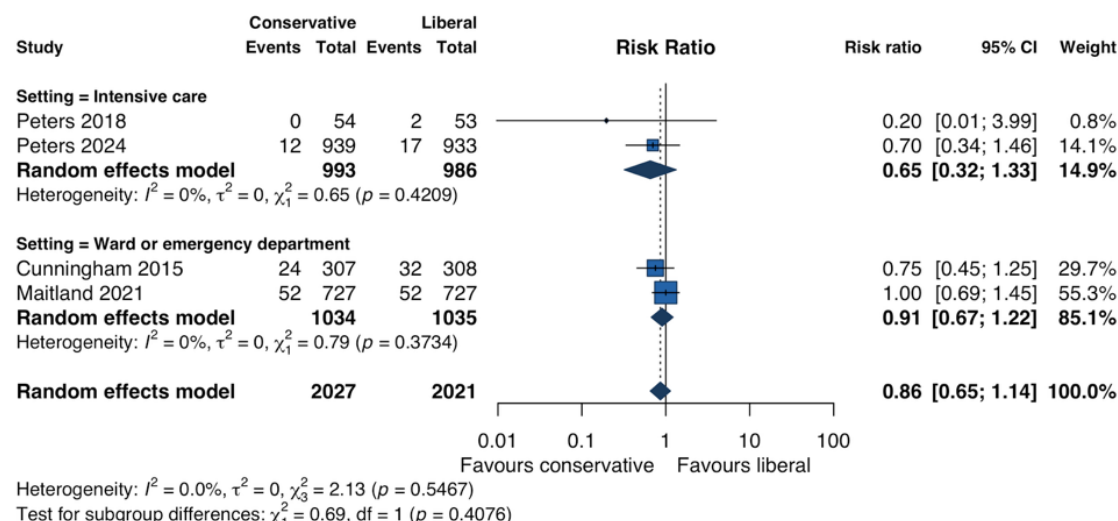


Figure 4. Children experiencing at least one serious adverse event, subgrouped by care setting.

Hospital length of stay

Six trials provided hospital length of stay for 4,685 children. The pooled standardised mean difference favoured conservative targets at -0.28 (95% CI -0.52 to -0.04), $p = 0.022$, with substantial heterogeneity ($I^2 = 86.9\%$, tau-squared = 0.070 , $Q = 38.19$, $df = 5$, $p < 0.001$), as illustrated in Figure 5.

The effect was concentrated outside intensive care. The standardised mean difference was -0.06 (95% CI -0.20 to 0.07) in the two intensive care trials ($I^2 = 23.9\%$) and -0.40

(95% CI -0.75 to -0.04) in the four ward or emergency trials ($I^2 = 88.2\%$), with a test for subgroup differences of $p = 0.087$. The largest single effect came from the Dutch threshold trial, in which median stay fell from 60.8 to 39.8 hours (standardised mean difference -0.57 , 95% CI -0.74 to -0.40),⁴¹ followed by the bronchiolitis trial, in which median stay fell from 50.9 to 40.9 hours.⁴⁰ In the definitive intensive care trial the mean duration of the index admission was 17.5 days with conservative and 18.6 days with liberal targets (standardised mean difference -0.03 , 95% CI -0.12 to 0.06).^{38,47}

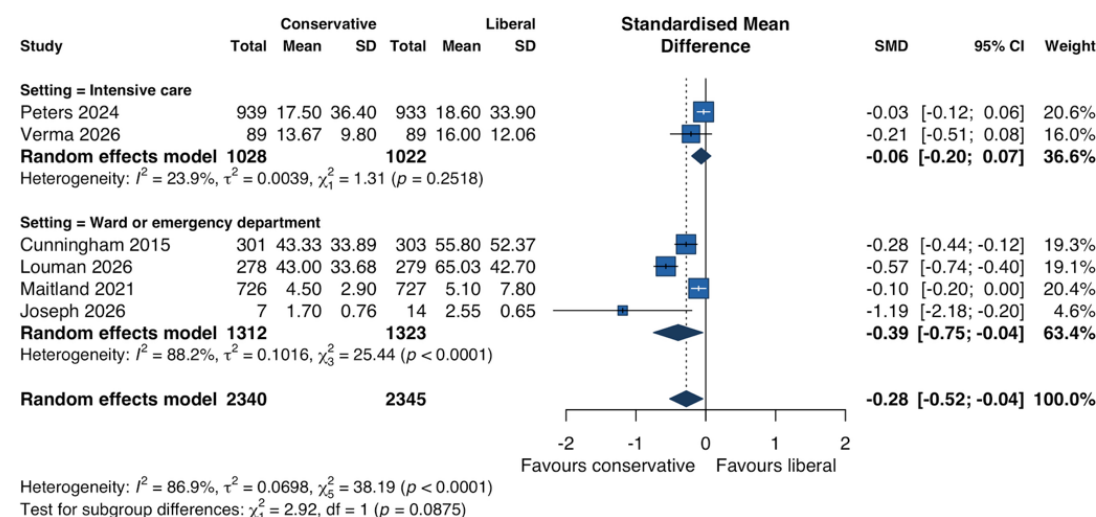


Figure 5. Hospital length of stay expressed as the standardised mean difference (Hedges g), subgrouped by care setting. Standardisation makes trials that measured stay in hours comparable with those that measured it in days. Negative values favour conservative targets.

Intensive care length of stay

Three intensive care trials reported length of stay in the unit for 2,104 children. Conservative targets were associated with a mean difference of -1.14 (95% CI -2.37 to 0.09) days, $p = 0.07$, with substantial heterogeneity ($I^2 = 70.4\%$, $Q = 6.77$, $df = 2$, $p = 0.034$), as illustrated in Figure 6. The estimate was largest in the Indian trial, in which median stay fell from 8 to 6 days (mean difference -2.50 days, 95% CI -4.26 to -0.74),³⁹

and smallest in the definitive trial, in which median stay among survivors fell from 5 to 4 days (mean difference -0.33 days, 95% CI -0.67 to 0.01).³⁸ Duration of respiratory support was also shorter with conservative targets in the Indian trial (median 4 versus 6 days, $p = 0.003$),³⁹ and time to liberation from invasive ventilation was shorter in the definitive trial.^{38,47}

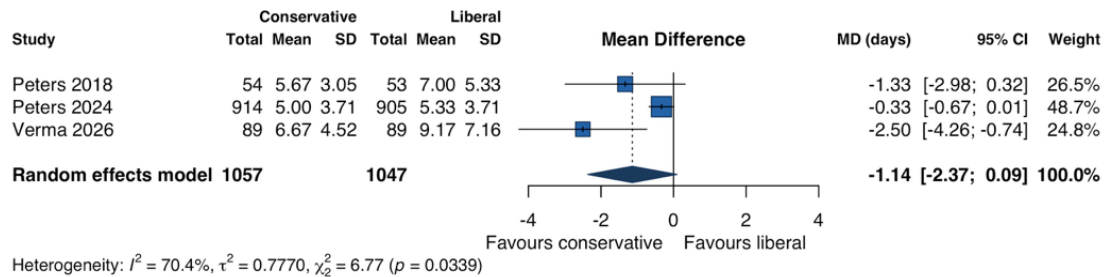


Figure 6. Length of stay in the paediatric intensive care unit, expressed as the mean difference in days.

Treatment failure and hospital admission

Two ward trials reported trial-defined treatment failure in 1,444 children. Failure was more frequent with conservative management (risk ratio 2.63 (95% CI 1.43 to 4.84), $p = 0.002$; $I^2 = 0.0\%$), as illustrated in Figure 7. The estimate was dominated by the African trial, in which 33 of 711 children managed with permissive hypoxaemia and 13 of 712 managed liberally met the failure definition of an SpO_2 below 92% with respiratory distress at 48 hours (risk ratio 2.54, 95% CI 1.35 to 4.79).⁴² Neither trial recorded a corresponding increase in death.

In the emergency department, lowering the effective oxygen threshold by three percentage points reduced hospitalisation within 72 hours from 44 of 108 to 26 of 105 infants with bronchiolitis (risk ratio 0.61 (95% CI 0.41 to 0.91)), without any intensive care admission or death in either arm.⁴⁴ The asthma trial reported hospitalisation of 25.5% with titrated oxygen and 40.5% with high-concentration oxygen, together with a smaller rise in transcutaneous carbon dioxide tension at 60 minutes, but exact numerators were not reported and the outcome could not be pooled.⁴⁵

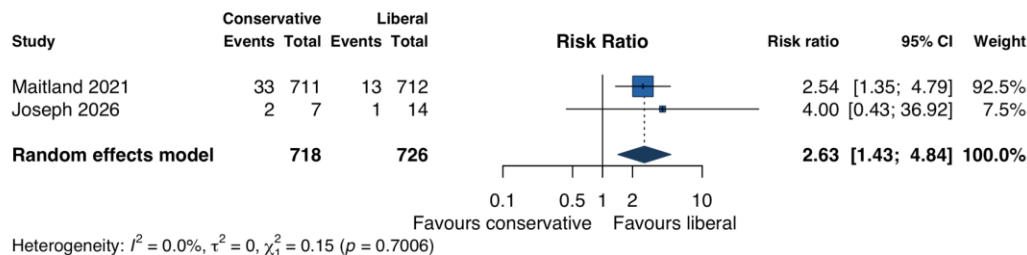


Figure 7. Trial-defined treatment failure, an exploratory safety outcome based on two trials only. Values above unity favour liberal targets.

Sensitivity analyses and small-study effects

The primary estimate was robust. Omitting each trial in turn produced pooled risk ratios between 0.93 and 1.11, all with confidence intervals crossing unity. Refitting the model as a common-effect analysis gave 0.98 (95% CI 0.71 to 1.35), a Peto odds ratio gave 0.98 (95% CI 0.69 to 1.37), and applying a 0.5 continuity correction to every trial gave 0.99 (95% CI 0.72 to 1.37), as detailed in Table 5; the treatment of sparse data therefore made no material difference to the estimate. For hospital length of stay, leave-one-out estimates ranged from

-0.20 to -0.34 , but restricting the analysis to the three trials that reported means and standard deviations directly attenuated the result to -0.29 (95% CI -0.92 to 0.33), $p = 0.36$.

Because no outcome was informed by ten or more trials, Egger's test was not performed. The funnel plot for mortality is presented in Figure 8 for completeness, but with six trials no inference about small-study effects is possible, and none is drawn.⁴⁸

Table 5. Sensitivity analyses.

Outcome	Analysis	Estimate (95% CI)	p value
All-cause mortality	Primary: Mantel-Haenszel RR, random effects (Paule-Mandel)	0.99 (0.72 to 1.37)	0.96
All-cause mortality	Mantel-Haenszel RR, common effect	0.98 (0.71 to 1.35)	0.88
All-cause mortality	Peto odds ratio (common effect)	0.98 (0.69 to 1.37)	0.88
All-cause mortality	Inverse-variance RR with 0.5 continuity correction, all studies	0.99 (0.72 to 1.37)	0.96
All-cause mortality	Leave-one-out range across the six trials	0.93 to 1.11	all $p > 0.05$
Hospital length of stay	Primary analysis (all six trials)	-0.28 (-0.52 to -0.04)	0.022
Hospital length of stay	Restricted to means reported directly (three trials)	-0.29 (-0.92 to 0.33)	0.36
Hospital length of stay	Leave-one-out range across the six trials	-0.34 to -0.20	—

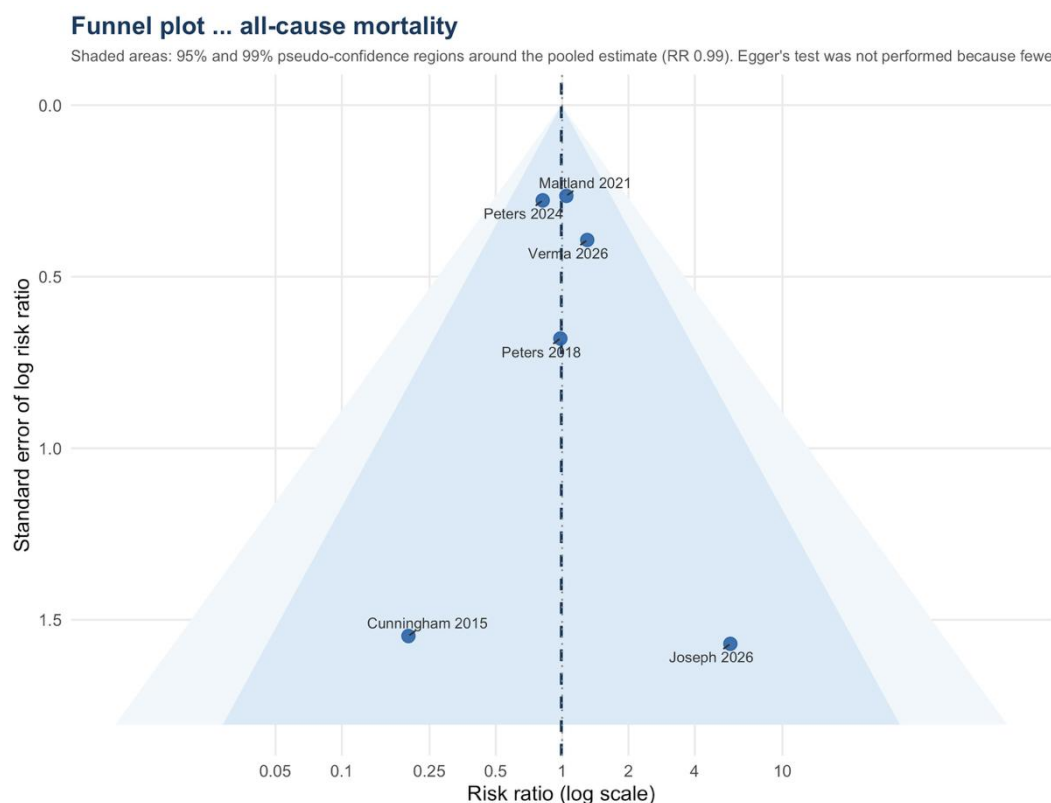


Figure 8. Funnel plot for all-cause mortality. Egger's test was not performed because fewer than ten trials contributed to the outcome.

Further sensitivity and meta-regression analyses

Restricting the mortality analysis to the four trials that reported death at 28 or 30 days gave a risk ratio of 0.97 (95% CI 0.70 to 1.36). Excluding the trial that used display-modified oximetry gave 1.01 (95% CI 0.73 to 1.40), excluding the permissive-hypoxaemia trial gave 0.96 (95% CI 0.63 to 1.45), and restricting the analysis to the four trials published from 2021 onwards gave 1.01 (95% CI 0.72 to 1.42); heterogeneity remained absent in every variant, as detailed in Table 6.

Hospital length of stay analysed as a ratio of means, which handles skewed stay data without standardisation, gave 0.80 (95% CI 0.71 to 0.90), corresponding to a stay 20% shorter with conservative targets ($p < 0.001$; $I^2 = 70.3\%$). The standardised estimate lost statistical significance when the display-modified oximetry trial was removed (-0.30 (95% CI -0.61 to 0.02), $p = 0.07$) and when the analysis was restricted to trials published from 2021 onwards (-0.30 (95% CI -0.61 to 0.02), $p = 0.07$), but was unchanged when the permissive-

hypoxaemia trial was removed (-0.33 (95% CI -0.62 to -0.04), $p = 0.02$).

Meta-regression did not identify a relationship between the treatment effect on mortality and the control-arm risk of death (coefficient 3.98, 95% CI -6.37 to 14.33 , $p = 0.45$), and the intensive care setting explained only 5.1% of the between-trial variance in hospital length of stay (coefficient 0.26, 95% CI -0.22 to 0.75 , $p = 0.28$; residual $I^2 = 88.5\%$). The setting-related difference in length of stay is therefore hypothesis-generating rather than established.

Confidence intervals around I^2 were wide for every secondary outcome, reflecting the small number of trials: 0% (95% CI 0 to 84.7) for serious adverse events, 86.9% (95% CI 73.8 to 93.5) for hospital length of stay and 70.4% (95% CI 0.0 to 91.3) for intensive care length of stay. Arm-specific and combined values for the two trials with three randomised groups are given in Table 7, and the certainty of evidence for each outcome is summarised in Table 8.

Table 6. Additional sensitivity analyses of the primary and principal secondary outcomes.

Analysis	Trials	Estimate (95% CI)	p value	I^2
Mortality — all six trials (primary analysis)	6	0.99 (0.72 to 1.37)	0.961	0.0%
Mortality — restricted to 28-day or 30-day timepoints	4	0.97 (0.70 to 1.36)	0.868	0.0%
Mortality — excluding the display-modified oximetry trial	5	1.01 (0.73 to 1.40)	0.951	0.0%
Mortality — excluding the permissive-hypoxaemia trial	5	0.96 (0.63 to 1.45)	0.843	0.0%
Mortality — trials published from 2021 onwards	4	1.01 (0.72 to 1.42)	0.943	0.0%
Hospital stay — all six trials (primary analysis)	6	-0.28 (-0.52 to -0.04)	0.022	86.9%
Hospital stay — excluding the display-modified oximetry trial	5	-0.30 (-0.61 to 0.02)	0.066	88.8%
Hospital stay — excluding the permissive-hypoxaemia trial	5	-0.33 (-0.62 to -0.04)	0.025	89.0%
Hospital stay — trials published from 2021 onwards	5	-0.30 (-0.61 to 0.02)	0.066	88.8%
Hospital stay — ratio of means (all six trials)	6	0.80 (0.71 to 0.90)	<0.001	70.3%

Mortality analyses are risk ratios; hospital-stay analyses are standardised mean differences except the final row, which is a ratio of means.

Table 7. Arm-specific and combined values for the two trials with three randomised groups.

Trial	Randomised group	n	Mean stay (days)	SD	Deaths / n
Maitland 2021	Permissive hypoxaemia (conservative)	726	4.5	2.9	28/718
Maitland 2021	Low-flow oxygen (liberal)	364	4.9	3.7	15/362
Maitland 2021	High-flow nasal therapy (liberal)	363	5.3	10.4	12/362
Joseph 2026	Standard care, no oxygen (conservative)	7	1.7	0.76	1/7
Joseph 2026	Low-flow nasal cannula (liberal)	7	2.7	0.76	0/7
Joseph 2026	High-flow nasal cannula (liberal)	7	2.4	0.53	0/7
Maitland 2021	Combined liberal arms as analysed	727	5.10	7.80	27/724
Joseph 2026	Combined liberal arms as analysed	14	2.55	0.65	0/14

Arms were combined with the standard formulae for pooling group means and standard deviations (Cochrane Handbook, section 6.5.2.10), so that no child contributed twice.

Table 8. Certainty of evidence for each outcome, assessed with the GRADE approach.

Outcome	Trials and participants	Effect estimate	Risk of bias	Inconsistency	Indirectness	Imprecision	Certainty
All-cause mortality	6 trials, 4,235 children	RR 0.99 (0.72 to 1.37)	Not serious	Not serious ($I^2 = 0\%$)	Not serious	Serious: 140 events; interval includes a 28% reduction and a 37% increase	Moderate
Serious adverse events	4 trials, 4,048 children	RR 0.86 (0.65 to 1.14)	Not serious	Not serious ($I^2 = 0\%$)	Serious: definitions differed between trials	Serious: 191 events	Low
Hospital length of stay	6 trials, 4,685 children	SMD -0.28 (-0.52 to -0.04)	Serious: outcome assessed by unblinded clinicians in four trials	Serious: $I^2 = 87\%$, unexplained by setting in meta-regression	Not serious	Serious: significance lost when restricted to directly reported means	Very low
Intensive care length of stay	3 trials, 2,104 children	MD -1.14 days (-2.37 to 0.09)	Serious: unblinded discharge decisions	Serious: $I^2 = 70\%$	Not serious	Serious: interval crosses no effect	Very low
Treatment failure	2 trials, 1,444 children	RR 2.63 (1.43 to 4.84)	Serious: unblinded assessment of a subjective threshold	Not serious ($I^2 = 0\%$)	Serious: definitions differed; both trials in low-resource wards	Serious: 49 events	Very low

All bodies of evidence began as high certainty because every included study was a randomised controlled trial. Publication bias could not be assessed because no outcome was informed by ten or more trials, and no outcome was rated down on that basis alone.

4. Discussion

Three findings emerged from this synthesis and they point in different directions, so the practical reading is stated at the outset: a lower saturation target did not change the number of children who died or suffered a serious adverse event; it shortened hospital stay outside intensive care by about one fifth; and it made a trial-defined treatment failure more likely in the two trials that measured it, without any of those failures translating into death. Taken together, these results support a lower target as a default where monitoring is reliable, and argue against it where it is not.

This synthesis of ten randomised trials and 5,171 children found that conservative oxygenation targets neither increased nor decreased mortality, that serious adverse events were similar between strategies, and that children managed to a lower target left hospital earlier, with the length-of-stay benefit confined to ward and emergency settings. The mortality estimate was stable: the pooled risk ratio of 0.99 sat almost exactly on the line of no effect, heterogeneity was absent, and no single trial moved the estimate outside the range 0.93 to 1.11. At the same time, the confidence interval remained compatible with a 28% relative reduction and a 37% relative increase in deaths, and the prediction interval was wider still, so the finding is best described as an absence of demonstrated harm rather than as demonstrated equivalence. In absolute terms the pooled risk difference was -0.4 percentage points (95% CI -1.2 to 0.4), so the data exclude neither a small benefit nor a small harm of roughly one death per hundred children treated.

These results align with the adult literature while adding a paediatric dimension that adult trials cannot supply. Lower oxygen targets did not change mortality in adults with acute hypoxaemic respiratory failure,¹⁷ in ventilated intensive care patients,^{18,19} or after cardiac arrest,^{20,21} and an individual patient

data meta-analysis produced a pooled risk ratio of 0.99, numerically identical to the present paediatric estimate.²⁴ The paediatric trials extend this picture to children in whom the physiological margins are narrower and, importantly, to settings where oxygen itself is scarce. The consistency of the result across an English intensive care network,³⁸ an Indian tertiary unit,³⁹ British and Dutch general wards,^{40,41} and East African district hospitals^{42,43} is the most clinically useful feature of this synthesis.

A biologically coherent explanation for the absence of harm is that the conservative targets tested were still comfortably above the steep portion of the oxyhaemoglobin dissociation curve, so that oxygen delivery was preserved while oxidative stress was reduced. Trials confirmed that separation between arms was real rather than nominal: time-weighted mean saturation differed by 2.7 percentage points and inspired oxygen fraction by 0.08 in the pilot intensive care trial,³⁷ duration of oxygen therapy fell from 100 to 8 hours in the Indian trial,³⁹ supplemental oxygen was given to 56% rather than 73% of infants with bronchiolitis,⁴⁰ and the Dutch threshold trial shortened oxygen exposure by more than a third.⁴¹ Reduced exposure plausibly shortened hospital stay by removing the requirement for an oxygen delivery device, a mechanism supported by the observation that lowering an institutional saturation goal to 88% shortened time to room air and length of stay without increasing readmission,⁴⁹ and by trials showing that shorter post-oxygen monitoring accelerated discharge safely.⁵⁰ Avoiding hyperoxia may also have attenuated the oxidative pathways demonstrated experimentally^{12,13,51} and in the randomised redox substudy.¹⁶

The exploratory excess of treatment failure demands attention rather than reassurance. Children managed conservatively were more than twice as likely to meet a trial-defined failure threshold, an effect driven by the African trial in which oxygen was withheld until saturation fell below 80%,

and which was stopped early after a public campaign against the permissive arm.⁴² That trial nonetheless showed that close monitoring allowed most children with moderate hypoxaemia to be weaned early and safely,⁵² which is precisely the point: a lower target is a monitoring strategy as much as an oxygen strategy. Where saturation is measured continuously and escalation is immediate, failure is detected and reversed; where oximetry is intermittent or absent, as in many facilities surveyed across Africa and Asia,^{27,28,53,54} the same target would be unsafe. This is the central qualification to the safety message of this review.

Heterogeneity in the length-of-stay analysis was substantial and was explained largely by setting. Trials in intensive care showed essentially no effect, while ward and emergency trials showed a moderate reduction, and the between-subgroup difference approached but did not reach conventional significance. This is clinically intelligible. In intensive care, discharge is governed by organ support, sedation and bed availability rather than by saturation, whereas on a general ward the saturation threshold is frequently the last criterion keeping a recovering child in hospital. Residual heterogeneity reflected the different comparators: a four percentage-point threshold difference in a Dutch ward population produced a much larger standardised effect than a permissive strategy in African children whose stay was dominated by the underlying pneumonia. Pooling days and hours as standardised effects also assumes a common underlying scale, an assumption that standardisation makes tolerable but does not eliminate.

The strengths of this review are the completeness of the search, which recovered two trials published after the most recent qualitative synthesis; the refusal to impute or back-calculate any value, with every pooled number traced to a published table; the use of the same conservative-versus-liberal framework across four care settings; and the breadth of the robustness checks, which included leave-one-out analysis, alternative effect measures for rare events, and a sensitivity analysis restricted to directly reported means.

Several limitations qualify these conclusions. First, only six trials contributed mortality data and 140 deaths occurred in total, so the analysis was underpowered for modest but clinically important differences, and random-effects inference with few trials is itself unreliable.³⁴ Second, the interventions were heterogeneous in kind as well as degree, ranging from an 88–92% target during mechanical ventilation to withholding oxygen entirely above 80%; the pooled estimate therefore describes a family of strategies rather than a single dose. Third, most trials were unblinded, and although mortality is robust to unblinding, length of stay and treatment failure are decided by clinicians who knew the allocation. Fourth, half of the length-of-stay data required conversion from medians, and the sensitivity analysis restricted to directly reported means lost statistical significance, so that result should be regarded as suggestive. Fifth, adverse-event definitions differed between trials despite restriction to serious events, and two trials could not contribute because per-arm counts were not retrievable.

Further limitations concern generalisability and measurement. Children with cyanotic congenital heart disease, pulmonary hypertension and chronic lung disease were excluded from most trials, and the findings do not extend to them. Pulse oximetry itself is imperfect: bias increases at lower saturations and with darker skin pigmentation, with occult hypoxaemia reported in 12% of Black compared with 6% of White children hospitalised with COVID-19,⁵⁵ and comparable discrepancies documented in adults and neonates.^{56–59} A target band of 88–92% therefore carries a different true arterial saturation in different children, a concern examined directly in

a post hoc analysis of the largest trial.⁶⁰ Finally, no outcome was informed by ten or more trials, so small-study effects could not be assessed formally and the possibility of unpublished neutral or negative trials cannot be excluded.

For clinical practice, these data support targeting an SpO₂ of approximately 88–92% in mechanically ventilated children and accepting a threshold of 90% rather than 94% for starting or continuing oxygen on a paediatric ward, provided saturation is monitored and escalation is immediately available. The likely benefits are shorter oxygen exposure, earlier discharge and reduced consumption of a resource that remains rationed in much of the world.^{28,29,32} For research, the priorities are adequately powered trials in ward and emergency populations, trials that pair a lower target with an explicit monitoring and escalation protocol, individual patient data analysis to identify children in whom a lower target is harmful, and the incorporation of oximeter performance across skin tones into target setting.

The further analyses sharpened this reading. Mortality was unchanged when the timepoint was restricted to 28 or 30 days, when the display-modified oximetry trial or the permissive-hypoxaemia trial was excluded, and when only trials published from 2021 onwards were retained, so the null result is not an artefact of pooling heterogeneous interventions or of older standards of supportive care. The length-of-stay finding was less robust: expressed as a ratio of means it corresponded to a stay 20% shorter with conservative targets, but the standardised estimate lost significance when the double-blind bronchiolitis trial was removed and when the analysis was restricted to trials that reported means directly. Meta-regression attributed almost none of the between-trial variance to the intensive care setting, so the setting explanation offered above remains a hypothesis rather than a demonstrated mechanism.

The choice of mortality as the review's primary outcome also deserves comment, because it is not the primary outcome of the largest trial, which ranked duration of organ support with death ranked worst and found a modest advantage for conservative targets (adjusted odds ratio 0.84, 95% CI 0.72 to 0.99).³⁸ A review that pooled mortality alone necessarily discarded that composite signal, which is why duration of respiratory support, time to liberation from ventilation and duration of oxygen therapy were summarised narratively: each favoured the conservative arm in the trials that measured it.^{38,39,41,47} The consistent direction of these process outcomes, alongside a flat mortality curve, is the strongest argument that lowering the target is at worst neutral and probably beneficial for resource use.

That resource argument matters most where oxygen is scarce. Conservative management reduced the duration of oxygen therapy from a median of 100 to 8 hours in the Indian intensive care trial,³⁹ reduced the proportion of infants receiving any supplemental oxygen from 73% to 56% in the bronchiolitis trial,⁴⁰ and shortened oxygen exposure by more than a third in the Dutch ward trial.⁴¹ In systems where a single concentrator serves a whole paediatric ward, where only a quarter of primary facilities have a functional pulse oximeter,²⁸ and where oxygen scale-up programmes have had to be financed as public health interventions in their own right,^{29–32,61} halving oxygen consumption without increasing mortality is a substantial gain. The same logic does not apply in well-resourced intensive care units, where the benefit is measured in avoided hyperoxia rather than in litres of gas.

Children with cyanotic congenital heart disease, pulmonary hypertension, chronic lung disease and sickle cell disease were excluded from all or nearly all of these trials, yet they are the children in whom clinicians deliberate about

oxygen targets most often. No randomised evidence addresses them. The nearest data come from cardiac surgery, where hyperoxia on cardiopulmonary bypass has been associated with operative mortality,^{10,11} where normoxic management proved feasible and reduced postoperative inflammation in a small randomised trial of cyanotic neonates,⁶² and where an experimental study found no difference in cerebral mitochondrial respiration between normoxic and hyperoxic bypass.⁶³ These populations were deliberately excluded here because their baseline saturation targets differ fundamentally, and the present results must not be extrapolated to them.

Two features of the evidence base limit how far any recommendation can travel. First, the interventions ranged from a target band during mechanical ventilation to the outright withholding of oxygen above a saturation of 80%; describing this family of strategies with a single pooled estimate is defensible only because heterogeneity for mortality was absent, and the permissive extreme was also the only strategy associated with excess treatment failure. Second, the oxygen-delivery modality differed between and within trials, with high-flow nasal therapy used as the liberal comparator in two trials; modality itself alters treatment failure and escalation independently of the saturation target,⁶⁴⁻⁶⁹ so part of the observed difference in treatment failure may reflect what was delivered rather than the target aimed for.

Finally, the certainty of this evidence should be read alongside its statistical presentation. Using GRADE, certainty was moderate for mortality, low for serious adverse events and very low for both length-of-stay outcomes and for treatment failure, as detailed in Table 8. Judging imprecision against the prediction interval rather than the confidence interval alone, as recent methodological work recommends,³⁵ reinforces that conclusion: the prediction interval for mortality extended from 0.65 to 1.52, so a future trial in a new setting could still show a clinically important difference in either direction. Evidence of this certainty supports a conditional recommendation and continued trials, not a change of standard.

5. Conclusion

Across ten randomised controlled trials and 5,171 acutely ill children, conservative oxygenation targets produced mortality and serious adverse-event rates that were indistinguishable from those of liberal targets, while shortening hospital stay in ward and emergency settings and reducing the duration of oxygen exposure in every trial that measured it. The pooled risk ratio for death of 0.99, with no detectable heterogeneity and stability under every sensitivity analysis performed, provides the most complete randomised evidence currently available on lowering the saturation target in children beyond the neonatal period, with a pooled absolute risk difference of -0.4 percentage points (95% CI -1.2 to 0.4) and moderate certainty by GRADE. The width of the confidence interval nonetheless means that this is evidence of absence of demonstrated harm rather than proof of equivalence, and the excess of trial-defined treatment failure with the most permissive strategy shows where the limits of safety lie.

The practical message is therefore conditional rather than universal. A conservative target is defensible, and probably preferable, wherever peripheral oxygen saturation is monitored continuously or frequently and additional oxygen can be delivered without delay; it should not be adopted where oximetry is intermittent, where staffing prevents timely escalation, or in children with cyanotic heart disease, pulmonary hypertension or chronic lung disease, who were excluded from these trials. Adequately powered trials outside

intensive care, explicit pairing of lower targets with monitoring and escalation protocols, individual patient data analyses to identify children who are harmed, and attention to oximeter performance across skin tones are the necessary next steps before a single paediatric oxygenation target can be recommended for every setting.

Stated as a single priority, the field needs an adequately powered randomised trial of a lower versus a higher saturation threshold on general paediatric wards, in which the lower target is paired with a defined monitoring and escalation protocol and treatment failure is measured with a common definition. Until such a trial reports, a conservative target should be adopted deliberately, with the monitoring that makes it safe, rather than by default.

Declarations

Ethics approval

This study synthesised aggregate data from previously published randomised controlled trials and did not involve individual-level or restricted data; therefore, ethics committee approval and informed consent were not required.

Consent for publication

Not applicable because this review used published aggregate data and contains no identifiable individual information.

PRISMA guideline statement

This systematic review and meta-analysis was prepared and reported in accordance with the PRISMA 2020 statement.

Data availability

All data analysed are contained in the published reports of the included trials and in the tables of this article. Additional extraction records and analytic materials are available from the corresponding author on reasonable request.

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Conflict of interest

The authors declare no financial or non-financial conflicts of interest related to this manuscript.

Author contributions

AIR: Conceptualisation; Methodology; Validation; Supervision; Project administration; Writing – original draft; Writing – review and editing. MYA: Investigation; Data curation; Formal analysis; Writing – review and editing. SRF: Investigation; Data curation; Validation; Writing – review and editing. CRJ: Investigation; Data curation; Visualisation; Writing – review and editing. ASN: Methodology; Resources; Validation; Writing – review and editing. ADY: Formal analysis; Software; Visualisation; Writing – review and editing. All authors met the ICMJE authorship criteria, approved the final manuscript, and accept accountability for the work.

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Use of artificial intelligence

No artificial intelligence (AI) tools were used in the preparation of this manuscript.

References

1. Rahman AE, Hossain AT, Chisti MJ, et al. Hypoxaemia prevalence and its adverse clinical outcomes among children hospitalised with WHO-defined severe pneumonia in Bangladesh. *J Glob Health*. 2021;11:04053. doi: 10.7189/jogh.11.04053.
2. Awasthi S, Rastogi T, Pandey AK, et al. Epidemiology of Hypoxic Community-Acquired Pneumonia in Children Under 5 Years of Age: An Observational Study in Northern India. *Front Pediatr*. 2021;9:790109. doi: 10.3389/fped.2021.790109.

3. Hoekstra NE, Joseph KS, Schuh HB, et al. Hypoxaemia and mortality in children with lower respiratory infection in low-income and middle-income countries: systematic review and meta-analysis. *Lancet Glob Health*. 2026;104031. doi: 10.1016/j.lanlco.2026.104031.
4. McCollum ED, Ahmed S, Roy AD, et al. Risk and accuracy of outpatient-identified hypoxaemia for death among suspected child pneumonia cases in rural Bangladesh: a multifacility prospective cohort study. *Lancet Respir Med*. 2023;11(9):769–781. doi: 10.1016/S2213-2600(23)00098-X.
5. Balcarcel DR, Coates BM, Chong G, et al. Excessive Oxygen Supplementation in the First Day of Mechanical Ventilation Is Associated With Multiple Organ Dysfunction and Death in Critically Ill Children. *Pediatr Crit Care Med*. 2022;23(2):89–98. doi: 10.1097/PCC.0000000000002861.
6. Bachman TE, Newth CJL, Ross PA, et al. Association of extreme hyperoxic events and mortality in pediatric critical care: an observational cohort study. *Front Pediatr*. 2024;12:1429882. doi: 10.3389/fped.2024.1429882.
7. Holton C, Lee BR, Escobar H, et al. Admission Pa o₂ and Mortality Among PICU Patients and Select Diagnostic Subgroups. *Pediatr Crit Care Med*. 2023;24(8):e362–e371. doi: 10.1097/PCC.0000000000003247.
8. Frazier AH, Topjian AA, Reeder RW, et al. Association of Pediatric Postcardiac Arrest Ventilation and Oxygenation with Survival Outcomes. *Ann Am Thorac Soc*. 2024;21(6):895–906. doi: 10.1513/AnnalsATS.202311-9480C.
9. Brohan O, Chenouard A, Gaultier A, et al. Pa o₂ and Mortality in Neonatal Extracorporeal Membrane Oxygenation: Retrospective Analysis of the Extracorporeal Life Support Organization Registry, 2015–2020. *Pediatr Crit Care Med*. 2024;25(7):591–598. doi: 10.1097/PCC.0000000000003508.
10. Beshish AG, Jahadi O, Mello A, et al. Hyperoxia During Cardiopulmonary Bypass Is Associated With Mortality in Infants Undergoing Cardiac Surgery. *Pediatr Crit Care Med*. 2021;22(5):445–453. doi: 10.1097/PCC.0000000000002661.
11. Beshish AG, Kwiatkowski DM, Sznycer-Taub N, et al. Hyperoxia During Neonatal Cardiopulmonary Bypass Is Associated With Worse Clinical Outcomes: A Multi-Institutional Study. *J Am Heart Assoc*. 2026;15(1):e045890. doi: 10.1161/JAHA.125.045890.
12. Harijith A, Basa P, Ha A, et al. NOX4 Mediates Epithelial Cell Death in Hyperoxic Acute Lung Injury Through Mitochondrial Reactive Oxygen Species. *Front Pharmacol*. 2022;13:880878. doi: 10.3389/fphar.2022.880878.
13. Chou HC, Chen CM. Hyperoxia Induces Ferroptosis and Impairs Lung Development in Neonatal Mice. *Antioxidants (Basel)*. 2022;11(4):641. doi: 10.3390/antiox11040641.
14. Koloko Ngassie ML, Thompson MA, Roos BB, et al. Hyperoxia-induced senescence in fetal airway smooth muscle cells: role of mitochondrial reactive oxygen species and endoplasmic reticulum stress. *Am J Physiol Lung Cell Mol Physiol*. 2025;329(1):L1–L18. doi: 10.1152/ajplung.00348.2024.
15. Lithopoulos MA, Toussay X, Zhong S, et al. Neonatal hyperoxia in mice triggers long-term cognitive deficits via impairments in cerebrovascular function and neurogenesis. *J Clin Invest*. 2022;132(22):e146095. doi: 10.1172/JCI146095.
16. Jones GAL, Eaton S, Orford M, et al. Randomization to a Liberal Versus Conservative Oxygenation Target: Redox Responses in Critically Ill Children. *Pediatr Crit Care Med*. 2023;24(3):e137–e146. doi: 10.1097/PCC.0000000000003175.
17. Schjørring OL, Klitgaard TL, Perner A, et al. Lower or Higher Oxygenation Targets for Acute Hypoxemic Respiratory Failure. *N Engl J Med*. 2021;384(14):1301–1311. doi: 10.1056/NEJMoa2032510.
18. Semler MW, Casey JD, Lloyd BD, et al. Oxygen-Saturation Targets for Critically Ill Adults Receiving Mechanical Ventilation. *N Engl J Med*. 2022;387(19):1759–1769. doi: 10.1056/NEJMoa2208415.
19. Martin DS, Gould DW, Shahid T, et al. Conservative Oxygen Therapy in Mechanically Ventilated Critically Ill Adult Patients: The UK-ROX Randomized Clinical Trial. *JAMA*. 2025;334(5):398–408. doi: 10.1001/jama.2025.9663.
20. Schmidt H, Kjaergaard J, Hassager C, et al. Oxygen Targets in Comatose Survivors of Cardiac Arrest. *N Engl J Med*. 2022;387(16):1467–1476. doi: 10.1056/NEJMoa2208686.
21. LOGICAL Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group, Hodgson CL, Mackle D, et al. Conservative Oxygen for Unresponsive Patients after Cardiac Arrest. *N Engl J Med*. 2026;395(6):571–581. doi: 10.1056/NEJMoa2513814.
22. Nielsen FM, Klitgaard TL, Siegmund M, et al. Lower vs Higher Oxygenation Target and Days Alive Without Life Support in COVID-19: The HOT-COVID Randomized Clinical Trial. *JAMA*. 2024;331(14):1185–1194. doi: 10.1001/jama.2024.2934.
23. Crescioli E, Nielsen FM, Bunzel AM, et al. Long-term mortality and health-related quality of life with lower versus higher oxygenation targets in intensive care unit patients with COVID-19 and severe hypoxaemia. *Intensive Care Med*. 2024;50(10):1603–1613. doi: 10.1007/s00134-024-07613-2.
24. Nielsen FM, Klitgaard TL, Bruun NH, et al. Lower or higher oxygenation targets in the intensive care unit: an individual patient data meta-analysis. *Intensive Care Med*. 2024;50(8):1275–1286. doi: 10.1007/s00134-024-07523-3.
25. Buell KG, Spicer AB, Casey JD, et al. Individualized Treatment Effects of Oxygen Targets in Mechanically Ventilated Critically Ill Adults. *JAMA*. 2024;331(14):1195–1204. doi: 10.1001/jama.2024.2933.
26. Louman S, Verlaet CWM, van Stralen KJ, et al. Oxygen saturation targets for children with respiratory distress: a systematic review. *ERJ Open Res*. 2023;9(5):00256–2023. doi: 10.1183/23120541.00256-2023.
27. Tuti T, Aluvaala J, Akech S, et al. Pulse oximetry adoption and oxygen orders at paediatric admission over 7 years in Kenya: a multihospital retrospective cohort study. *BMJ Open*. 2021;11(9):e050995. doi: 10.1136/bmjopen-2021-050995.
28. Subhi R, Burhin M, Lam F, et al. Medical oxygen service readiness and service coverage in seven countries in Africa and Asia: a cross-sectional survey and clinical audit. *Lancet Glob Health*. 2025;13(10):e1701–e1714. doi: 10.1016/S2214-109X(25)00328-6.
29. Duke T, Pulsan F, Panauwe D, et al. Solar-powered oxygen, quality improvement and child pneumonia deaths: a large-scale effectiveness study. *Arch Dis Child*. 2021;106(3):224–230. doi: 10.1136/archdischild-2020-320107.
30. Graham HR, Bakare AA, Ayede AI, et al. Cost-effectiveness and sustainability of improved hospital oxygen systems in Nigeria. *BMJ Glob Health*. 2022;7(8):e009278. doi: 10.1136/bmjgh-2022-009278.
31. Graham HR, Kitutu FE, Kamuntu Y, et al. Improving effective coverage of medical-oxygen services for neonates and children in health facilities in Uganda: a before-after intervention study. *Lancet Glob Health*. 2024;12(9):e1506–e1516. doi: 10.1016/S2214-109X(24)00268-7.
32. Huang Y, Mian Q, Conradi N, et al. Estimated Cost-effectiveness of Solar-Powered Oxygen Delivery for Pneumonia in Young Children in Low-Resource Settings. *JAMA Netw Open*. 2021;4(6):e2114686. doi: 10.1001/jamanetworkopen.2021.14686.
33. Tang X, Tong T, Zhang X, et al. Minimum distance estimation of mean and standard deviation from reported quantiles. *Res Synth Methods*. 2026;17(5):958–975. doi: 10.1017/rsm.2026.10090.
34. Duan Y, Mathew T, Alemayehu D, et al. Novel approaches for random-effects meta-analysis of a small number of studies under normality. *Res Synth Methods*. 2025;16(6):922–936. doi: 10.1017/rsm.2025.10022.
35. Murad MH, Morgan RL, Falck-Ytter Y, et al. Simultaneous evaluation of the imprecision and inconsistency domains of GRADE can be performed using prediction intervals. *J Clin Epidemiol*. 2024;175:111543. doi: 10.1016/j.jclinepi.2024.111543.
36. Djulbegovic B, Koletsis D, Hozo I, et al. High certainty evidence is stable and trustworthy, whereas evidence of moderate or lower certainty may be equally prone to being unstable. *J Clin Epidemiol*. 2024;171:111392. doi: 10.1016/j.jclinepi.2024.111392.
37. Peters MJ, Jones GAL, Wiley D, et al. Conservative versus liberal oxygenation targets in critically ill children: the randomised multiple-centre pilot Oxy-PICU trial. *Intensive Care Med*. 2018;44(8):1240–1248. doi: 10.1007/s00134-018-5232-7.
38. Peters MJ, Gould DW, Ray S, et al. Conservative versus liberal oxygenation targets in critically ill children (Oxy-PICU): a UK multicentre, open, parallel-group, randomised clinical trial. *Lancet*. 2024;403(10424):355–364. doi: 10.1016/S0140-6736(23)01968-2.
39. Verma S, Sahoo MR, Jindal A, et al. Conservative versus conventional oxygenation target in children admitted in PICU: a randomized controlled trial. *Eur J Pediatr*. 2026;185(4):203. doi: 10.1007/s00431-026-06876-9.
40. Cunningham S, Rodriguez A, Adams T, et al. Oxygen saturation targets in infants with bronchiolitis (BIDS): a double-blind, randomised, equivalence trial. *Lancet*. 2015;386(9998):1041–1048. doi: 10.1016/S0140-6736(15)00163-4.
41. Louman S, van Stralen KJ, Koppelman GH, et al. Oxygen saturation thresholds in children with acute respiratory distress (OxyKids): a multicentre, open, parallel-group, randomised clinical trial. *Lancet Respir Med*. 2026;14(8):673–682. doi: 10.1016/S2213-2600(26)00087-1.
42. Maitland K, Kiguli S, Olupot-Olupot P, et al. Randomised controlled trial of oxygen therapy and high-flow nasal therapy in African children with pneumonia. *Intensive Care Med*. 2021;47(5):566–576. doi: 10.1007/s00134-021-06385-3.
43. Joseph KS, Mvalo T, Shilkofski N, et al. Oxygen therapy for children with an oxygen saturation of 90–93% in Malawi: the NoGoLO2 pilot randomised controlled trial. *BMJ Paediatr Open*. 2026;10(1):e004256. doi: 10.1136/bmjpo-2025-004256.
44. Schuh S, Freedman S, Coates A, et al. Effect of oximetry on hospitalization in bronchiolitis: a randomized clinical trial. *JAMA*. 2014;312(7):712–718. doi: 10.1001/jama.2014.8637.
45. Patel B, Khine H, Shah A, et al. Randomized clinical trial of high concentration versus titrated oxygen use in pediatric asthma. *Pediatr Pulmonol*. 2019;54(7):970–976. doi: 10.1002/ppul.24329.
46. Singhi SC, Baranwal AK, Guruprasad, et al. Potential risk of hypoxaemia in patients with severe pneumonia but no hypoxaemia on initial assessment: a prospective pilot trial. *Paediatr Int Child Health*. 2012;32(1):22–26.

- doi: 10.1179/2046905511Y.0000000001.
47. Gould D, Ray S, Chang I, et al. Conservative versus liberal oxygenation targets in critically ill children: the Oxy-PICU RCT. *Health Technol Assess.* 2026;30(13):1–20. doi: 10.3310/HHYY5898.
 48. Al Amer FM, Lin L. Prediction Performance of Earlier Studies for Later Studies in Cochrane Reviews. *J Eval Clin Pract.* 2025;31(4):e70172. doi: 10.1111/jep.70172.
 49. Briggs S, Gupta V, Thakkar N, et al. Decreasing Goal Oxygen Saturations in Bronchiolitis Is Associated With Decreased Length of Stay. *Hosp Pediatr.* 2023;13(8):688–694. doi: 10.1542/hpeds.2022-007020.
 50. Gilbert Y, Shrapnel J, Lau C, et al. Duration of monitoring after cessation of oxygen therapy in infants with bronchiolitis. *J Paediatr Child Health.* 2023;59(11):1223–1229. doi: 10.1111/jpc.16485.
 51. Beyer AM, Norwood Toro LE, Hughes WE, et al. Autophagy, TERT, and mitochondrial dysfunction in hyperoxia. *Am J Physiol Heart Circ Physiol.* 2021;321(5):H985–H1003. doi: 10.1152/ajpheart.00166.2021.
 52. Maitland K, Giallongo E, Hamaluba M, et al. Early weaning from oxygen therapy in African children with severe pneumonia. *BMC Med.* 2025;23(1):366. doi: 10.1186/s12916-025-04178-9.
 53. Tolla HS, Asemere YA, Desale AY, et al. Changes in the availability of medical oxygen and its clinical practice in Ethiopia during a national scale-up program: a time series design from thirty-two public hospitals. *BMC Pediatr.* 2021;21(1):451. doi: 10.1186/s12887-021-02844-4.
 54. Colbourn T, Falade AG, Graham HR, et al. Pulse oximetry and oxygen services for under-five children with community-acquired pneumonia attending primary and secondary level health facilities in Lagos, Nigeria (INSPIRING-Lagos): a pre-implementation and post implementation study. *BMJ Public Health.* 2024;2(2):e001210. doi: 10.1136/bmjph-2024-001210.
 55. Savorgnan F, Hassan A, Borges N, et al. Pulse Oximetry and Arterial Saturation Difference in Pediatric COVID-19 Patients: Retrospective Analysis by Race. *Pediatr Crit Care Med.* 2023;24(6):458–462. doi: 10.1097/PCC.0000000000003208.
 56. Seitz KP, Wang L, Casey JD, et al. Pulse Oximetry and Race in Critically Ill Adults. *Crit Care Explor.* 2022;4(9):e0758. doi: 10.1097/CCE.0000000000000758.
 57. Martin DS, Doidge JC, Gould D, et al. The impact of skin tone on performance of pulse oximeters used by NHS England COVID Oximetry @home scheme: measurement and diagnostic accuracy study. *BMJ.* 2026;392:e085535. doi: 10.1136/bmj-2025-085535.
 58. Saïdy S, Iqbal A, Baig SH. Pulse Oximetry Discrepancies and Occult Hypoxemia in ICU Patients: Predictors and Clinical Outcomes. *J Intensive Care Med.* 2025;40(12):1269–1278. doi: 10.1177/08850666251351594.
 59. Sudat SEK, Wesson P, Rhoads KF, et al. Racial Disparities in Pulse Oximeter Device Inaccuracy and Estimated Clinical Impact on COVID-19 Treatment Course. *Am J Epidemiol.* 2023;192(5):703–713. doi: 10.1093/aje/kwac164.
 60. Jones GAL, Wiegand M, Ray S, et al. Ethnicity and observed oxygen saturations, fraction of inspired oxygen, and clinical outcomes: a post hoc analysis of the Oxy-PICU trial of conservative oxygenation. *Pediatr Crit Care Med.* 2024;25(11):e438–e446. doi: 10.1097/PCC.0000000000003583.
 61. Ali MM, Njiru HN, Al Azad A, et al. Survival of hypoxaemic patients treated with solar-powered oxygen in rural Somalia hospitals: a prospective, observational study. *EBioMedicine.* 2026;126:106196. doi: 10.1016/j.ebiom.2026.106196.
 62. Sznycer-Taub N, Peng YW, Yu S, et al. Perioperative Normoxia vs Hyperoxia in Neonates With Cyanotic Heart Disease Undergoing Cardiac Surgery: A Randomized Controlled Trial. *Ann Thorac Surg.* 2025;120(5):898–906. doi: 10.1016/j.athoracsur.2025.04.009.
 63. Aronowitz DI, Geoffrion TR, Piel S, et al. Normoxic Management during Cardiopulmonary Bypass Does Not Reduce Cerebral Mitochondrial Dysfunction in Neonatal Swine. *Int J Mol Sci.* 2024;25(10):5466. doi: 10.3390/ijms25105466.
 64. Ramnarayan P, Richards-Belle A, Drikite L, et al. Effect of High-Flow Nasal Cannula Therapy vs Continuous Positive Airway Pressure Therapy on Liberation From Respiratory Support in Acutely Ill Children Admitted to Pediatric Critical Care Units: A Randomized Clinical Trial. *JAMA.* 2022;328(2):162–172. doi: 10.1001/jama.2022.9615.
 65. Ramnarayan P, Richards-Belle A, Drikite L, et al. Effect of High-Flow Nasal Cannula Therapy vs Continuous Positive Airway Pressure Following Extubation on Liberation From Respiratory Support in Critically Ill Children: A Randomized Clinical Trial. *JAMA.* 2022;327(16):1555–1565. doi: 10.1001/jama.2022.3367.
 66. Kandasamy S, Rameshkumar R, Sangaralingam T, et al. High-flow nasal oxygen in infants and children for early respiratory management of pneumonia-induced acute hypoxemic respiratory failure: the CENTURI randomized clinical trial. *Intensive Care Med Paediatr Neonatal.* 2024;2(1):15. doi: 10.1007/s44253-024-00031-8.
 67. Maya M, Rameshkumar R, Selvan T, et al. High-Flow Nasal Cannula Versus Nasal Prong Bubble Continuous Positive Airway Pressure in Children With Moderate to Severe Acute Bronchiolitis: A Randomized Controlled Trial. *Pediatr Crit Care Med.* 2024;25(8):748–757. doi: 10.1097/PCC.0000000000003521.
 68. Eşki A, Öztürk GK, Turan C, et al. High-flow nasal cannula oxygen in children with bronchiolitis: A randomized controlled trial. *Pediatr Pulmonol.* 2022;57(6):1527–1534. doi: 10.1002/ppul.25893.
 69. Feng Y, Wang J, Yin Y, et al. Non-invasive respiratory support in pediatric patients with acute hypoxemic respiratory failure: a systematic review and network meta-analysis of randomized controlled trials. *EClinicalMedicine.* 2025;89:103550. doi: 10.1016/j.eclinm.2025.103550.