

Targeted Oxygen for Initial Resuscitation of Preterm Infants

The TORPIDO 30/60 Randomized Clinical Trial

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IMPORTANCE The most effective initial fraction of inspired oxygen (FIO₂) for resuscitating preterm newborns is unknown.

OBJECTIVE To compare outcomes of newborns born at 23 to 28 weeks' gestation resuscitated with initial FIO₂ of 0.6 vs 0.3.

DESIGN, SETTING, AND PARTICIPANTS Randomized clinical trial conducted in 31 maternity hospitals in 6 countries. Consent by waiver was obtained in Australia, certain institutions in India, and Malaysia; prospective informed consent was obtained in certain institutions in India and all institutions in Singapore, Spain, and the US. Infants due at 23 to 28 weeks' gestation were randomized shortly before birth. Those with congenital abnormalities affecting oxygenation, neurodevelopment, or survival were excluded. Randomization was conducted from September 2018 to September 2024, with follow-up expected to close in September 2026.

INTERVENTION Infants were randomized (1:1) to receive an initial FIO₂ of 0.6 or 0.3; FIO₂ was titrated to meet standard targets for oxygen saturation by pulse oximetry in the first 10 minutes or for clinical needs. Clinicians and those assessing outcomes were not blinded to group assignment.

MAIN OUTCOMES AND MEASURES The primary outcome was death and brain injury at 36 weeks' corrected gestational age; secondary outcomes were the individual components of the primary outcome.

RESULTS A total of 1641 newborns were randomized. The primary analysis included 728 newborns randomized to receive an FIO₂ of 0.6 and 741 to an FIO₂ of 0.3 after excluding 172 newborns, mostly for birth after 28 weeks' gestation and transfer to another hospital before birth (54% female). Rates of escalation to FIO₂ of 1.0 were similar between the groups (FIO₂ of 0.6: 41%; FIO₂ of 0.3: 38%). Primary outcome information was ascertained in 1423 newborns (96.9%). Death or brain injury at 36 weeks' corrected gestational age occurred in 330 of 703 newborns (46.9%) assigned to the FIO₂ of 0.6 group vs 344 of 720 (47.8%) assigned to the FIO₂ of 0.3 group (relative risk, 0.98 [95% CI, 0.89-1.09]).

CONCLUSIONS AND RELEVANCE Initiating resuscitation of preterm infants with FIO₂ of 0.6 vs 0.3 did not affect the risk of death or brain injury by 36 weeks' corrected gestational age. These results lay a foundation for future trials evaluating the effectiveness and safety of using higher initial FIO₂ levels for preterm infant resuscitation.

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The optimal concentration of oxygen to initiate respiratory support of preterm infants at birth remains controversial. Before the 1990s, pure oxygen (fraction of inspired oxygen [FiO_2] of 1.0) was standard based on the assumption that newborn cardiorespiratory depression was due to hypoxia.¹ In the 1990s, Saugstad and others showed that using air (FiO_2 of 0.21) instead of FiO_2 of 1.0 for full-term or near-full-term infants reduced time to first breath and oxidative injury without adverse neurodevelopmental outcomes.²⁻⁴ Meta-analyses of 5 trials (N = 1302) found reduced mortality with air compared with FiO_2 of 1.0.^{5,6}

Initial global recommendations to begin resuscitation with air or low FiO_2 ^{7,8} were largely based on studies of full-term asphyxiated infants, in whom the use of FiO_2 of 1.0 was associated with oxidative injury. However, these early trials did not involve titration of FiO_2 or monitoring of oxygen saturation as measured by pulse oximetry (SpO_2), and they predated the widespread use of pulse oximetry in the delivery room.⁹

By 2006, expert guidelines suggested using air for full-term infants⁷ and, in 2007, the Australian Resuscitation Council recommended air for all gestational ages.⁸ In 2010, international guidance recommended adjusting FiO_2 to target SpO_2 from healthy infants¹⁰ after initiating resuscitation with FiO_2 of 0.21 to 0.3 and avoiding FiO_2 greater than 0.65.⁹ There were no further changes to guidance after this.

The TORPIDO study, published in 2017,¹¹ was a randomized clinical trial of FiO_2 of 0.21 vs 1.0 for initial resuscitation of preterm infants with the primary outcome of death and/or disability at 2 years. The trial was halted early (n = 290) because of slow enrollment due to clinicians' reluctance to accept that infants might be assigned to receive an FiO_2 of 1.0.¹² Although no difference was seen in the primary outcome, an exploratory analysis suggested increased mortality in infants less than 29 weeks' gestation initially undergoing resuscitation with FiO_2 of 0.21 (odds ratio, 3.9 [95% CI, 1.1-13.4]).¹¹

The current trial, Targeted Oxygen for Initial Resuscitation of Preterm Infants (TORPIDO 30/60), was initiated to test the hypothesis that, for infants born at less than 29 weeks' gestation, initiating respiratory support at birth with FiO_2 of 0.6 compared with FiO_2 of 0.3 would improve survival without brain injury at 36 weeks' corrected gestational age. These FiO_2 concentrations were selected to fall within the parameters of current clinical guidance⁹ and were also based on meta-analyses that found differences in physiological and early clinical measures at lower or higher concentrations of oxygen.¹³

Methods

Trial Design and Oversight

This randomized, clinical, parallel, 2-group superiority trial was conducted in 31 maternity hospitals in 6 countries (8 in Australia, 13 in India, 1 in Malaysia, 2 in Singapore, 6 in Spain, and 1 in the US) (see [Supplement 1](#) for the trial protocol). The trial was approved by the Hunter New England Human Research Ethics Committee, Newcastle, Australia, as well as the relevant local ethics committee for each site. Parents or guardians provided written informed consent via 1 of 2 consent pro-

Key Points

Question Does initiating resuscitation of extremely preterm newborns with a higher level of fraction of inspired oxygen (FiO_2 ; 0.6) reduce risk of death or brain injury compared with a lower FiO_2 (0.3)?

Findings This randomized clinical trial of 1469 infants born at 23 to 28 weeks' gestation in 6 countries found no association between initial FiO_2 and death or brain injury at 36 weeks' corrected gestational age (46.9% vs 47.8%).

Meaning There was no difference in risk of brain injury or death after initiating resuscitation with an FiO_2 of 0.6 vs 0.3.

cesses depending on local ethics regulations. All sites in Australia and most in India recruited under a consent waiver process for randomization and the primary outcome. Other sites used prospective consent. The study was conducted and reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) 2010 reporting guideline. The trial was coordinated by the National Health and Medical Research Centre Clinical Trials Centre, University of Sydney, and overseen by an independent data and safety monitoring committee (DSMC). The DSMC remained blinded unless unblinded data review was required and provided independent oversight according to prespecified Haybittle-Peto criteria.^{14,15} The DSMC reviewed trial safety and interim data after approximately 50% of newborns were enrolled and recommended no changes in plan.

Participants

Newborns were eligible if they were born at 23 to 28 weeks' gestation and required respiratory support at birth (**Figure 1**). Those with major cardiopulmonary abnormalities or congenital malformations that could affect neurodevelopmental outcome or survival were excluded.

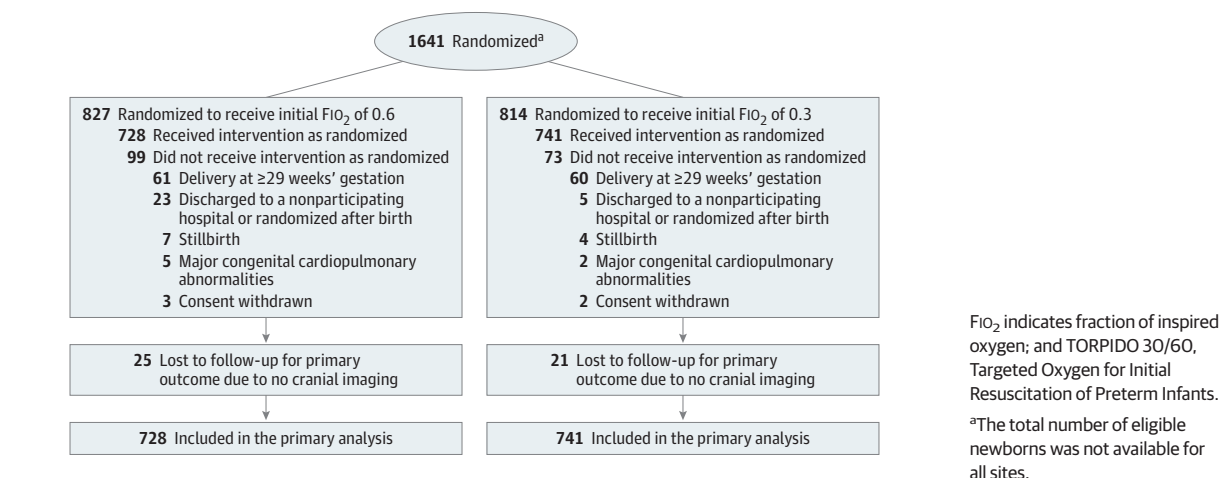
Randomization

Randomization was stratified by site, gestational age (<26 and ≥ 26 weeks' gestation), and pregnancy multiplicity using Flexetrial and occurred immediately before birth, when delivery was considered inevitable. Multiple births were assigned to the same treatment group. Newborns were deemed ineligible for inclusion after randomization if delivery did not occur by 28 weeks' gestation or if the parent was transferred to a nonparticipating hospital before delivery.

Trial Interventions

Infants born alive and eligible for active care were placed on the resuscitation bed after the umbilical cord was cut. Initial FiO_2 (0.6 or 0.3) was delivered via an oxygen blender. The trial protocol required that the initial level of FiO_2 at 0.3 or 0.6 be maintained for at least 5 minutes, if possible, to maintain separation between the groups, and then adjusted in 0.1 to 0.2 aliquots every 30 to 60 seconds using pulse oximetry to achieve targets of SpO_2 of 80% to 85% at 5 minutes and of SpO_2 of 85% to 95% at 10 minutes and until admission to the neonatal intensive care unit (NICU), according to the protocol

Figure 1. Randomization and Patient Flow in the TORPIDO 30/60 Trial



(Supplement 1) and international guidance.⁹ Escalation of FiO₂ to 1.0 could be made before or after 5 minutes if there were clinical concerns (eg, heart rate <100/minute and not increasing, additional resuscitation maneuvers such as cardiac massage required). Parents were masked to the study intervention group, but staff in the delivery room were not masked because FiO₂ had to be adjusted to meet SpO₂ targets. Equipment (blenders and oxygen analyzers) was visible to the clinicians.

Other elements of care were initiated according to local practice, including respiratory support with continuous positive airway pressure or ventilation. A pulse oximeter probe was applied to the right wrist before connecting the sensor to minimize delay in readout.¹⁶ Timing of cord clamping was recorded.

Time 0 of life was defined as delivery of the newborn. Transport of the newborn to the NICU occurred at the clinician's discretion, usually when the newborn was clinically stable (eg, SpO₂ of 85%-95% and heart rate >100/minute). During transfer, FiO₂ was adjusted to maintain SpO₂ of 85% to 95%. Management after admission was at the discretion of the clinical team.

Trial Outcomes

The primary outcome was death and brain injury at 36 weeks' corrected gestational age. Brain injury was defined by neuroimaging as any of the following: intraventricular hemorrhage (any grade), echodense intraparenchymal lesions, periventricular leukomalacia, or porencephalic cysts. All imaging scans were reported by a radiologist who was masked to study intervention. Secondary outcomes included the 2 components of the primary outcome, ie, all-cause mortality and brain injury at 36 weeks' corrected gestation. Predefined exploratory outcomes reported in this article are SpO₂ less than 80% or greater than or equal to 80% by 5 minutes of life, time to reach SpO₂ greater than or equal to 80%, heart rate less than 100/minute or greater than or equal to 100/minute at 5 minutes of age, intubation in delivery room, and Apgar score at 1 and 5 minutes. Exploratory outcomes added post hoc were use of cardiac massage and epinephrine, changes in FiO₂ in the first 10

Table 1. Maternal and Newborn Characteristics

Characteristic	No. (%)	
	FiO ₂ of 0.6	FiO ₂ of 0.3
Maternal	n = 592	n = 606
Age, mean (SD), y	32 (6)	32 (6)
Primigravida	293 (49)	296 (49)
Premature rupture of membranes (>24 h)	194 (33)	206 (34)
Any prenatal care	576 (97)	584 (96)
Chorioamnionitis	268 (28)	173 (29)
Magnesium sulfate	529 (89)	547 (90)
No antenatal steroids	23 (4)	14 (2)
Newborn	n = 728	n = 741
Female	387 (53)	410 (55)
Male	341 (47)	331 (45)
Gestation, mean (SD), wk	27 (2)	27 (2)
Gestation <26 wk	238 (33)	252 (34)
Birth weight, mean (SD), g	911 (242)	889 (228)
Multiple birth	180 (25)	184 (25)
Cesarean delivery	429 (59)	433 (58)

Abbreviation: FiO₂, fraction of inspired oxygen.

minutes after birth, and specific type of brain injury (eg, ventriculomegaly).

Other predefined exploratory outcomes not reported in this article were bronchopulmonary dysplasia, defined as survival to 36 weeks and requirement for supplemental oxygen or respiratory support; retinopathy of prematurity, defined as stage 3 or 4 and/or requiring surgical or medical intervention; necrotizing enterocolitis associated with surgery or death, measured to hospital discharge; late-onset sepsis with a culture-positive body fluid patent ductus arteriosus requiring medical or surgical treatment; duration of hospitalization; and survival without major disability at 2 to 3 years' corrected gestational age, assessed with either the Bayley Scales of Infant Development (version III and, after 2021, IV and V) and/or the Ages and Stages Questionnaire and a 28-item short child health questionnaire parent form.¹⁷⁻¹⁹

Table 2. Primary, Secondary, and Exploratory Brain Injury Outcomes^a

Outcome	No./total No. (%)		Absolute risk difference (95% CI)	Adjusted relative risk (95% CI)
	FiO ₂ of 0.6 (n = 728)	FiO ₂ of 0.3 (n = 741)		
Primary outcome				
Death and/or brain injury by 36 weeks' gestation	330/703 (46.9)	344/720 (47.8)	-0.84 (-6.02 to 4.35)	0.98 (0.89 to 1.09)
Secondary outcomes				
Death by 36 weeks' gestation	112/728 (15.4)	117/741 (15.8)	-0.40 (-4.11 to 3.30)	1.00 (0.79 to 1.27)
Any brain injury by 36 weeks' gestation	281/662 (42.4)	290/672 (43.2)	-0.71 (-6.02 to 4.60)	0.99 (0.87 to 1.1)
Exploratory brain injury outcomes^b				
Any intraventricular hemorrhage	212/706 (30.4)	216/719 (30.9)	-0.49 (-5.32 to 4.35)	0.98 (0.84 to 1.15)
Intraventricular hemorrhage grade 3 or 4	70/697 (10)	54/699 (8.0)	2.32 (-0.67 to 5.30)	1.30 (0.93 to 1.82)
Echodense intraparenchymal lesions	11/610 (1.8)	5/620 (0.8)	-0.92 (-2.90 to 1.06)	2.24 (0.74 to 6.77)
Periventricular leukomalacia	17/610 (2.8)	23/620 (3.7)	-0.92 (-2.90 to 1.06)	0.75 (0.39 to 1.43)
Porencephalic cysts	9/610 (1.5)	6/620 (1.0)	0.51 (-0.72 to 1.74)	1.52 (0.55 to 4.24)
Ventriculomegaly	39/610 (6.4)	16/620 (2.6)	3.81 (1.50 to 6.12)	2.48 (1.34 to 4.57)
Other brain injury ^c	142/610 (23.3)	129/620 (20.8)	2.44 (-2.20 to 7.07)	1.12 (0.90 to 1.40)

Abbreviation: FiO₂, fraction of inspired oxygen.

^a Outcomes were adjusted for multiple births and for stratification factors with gestation (<26 and ≥26 weeks' gestation).

^b Any brain injury included all of the exploratory brain injury outcomes, and imaging follow-up schedules were the same.

^c Other brain injuries include subdural and subarachnoid hemorrhage, infarcts, and ischemic lesions. Multiple brain pathologies can occur in 1 infant.

Adverse events were defined as any untoward medical occurrence in a patient; such occurrences did not necessarily have a causal relationship with a trial intervention. Adverse events were recorded but not required to be reported to trial-related committees. Suspected unexpected serious adverse reactions were reported within 30 days to the trial management committee and ethics boards and reviewed by the DSMC.

Sample Size and Power

A total of 1470 newborns (735 per group) were needed to detect a difference in brain injury-free survival from 24% to 32% (25% relative risk [RR] reduction), assuming 85% power, 5% significance, 10% nonadherence, and clustering from multiple births (intracluster correlation, 0.3; mean cluster size, 1.15). Sample size assumptions were reviewed at interim analysis and not modified.

Statistical Analysis

A statistical analysis plan was finalized before the data were unblinded and is available in [Supplement 2](#). Analyses followed the intention-to-treat principle and excluded stillbirths ([Supplement 2](#)). The primary and secondary outcomes were analyzed with a linear model with a log link, accounting for multiple births and adjusting for stratification factors used for randomization, including gestation (<26 and ≥26 weeks' gestation) and multiple births when the number of events was sufficient to allow this. Stratification factors were selected to minimize differences between the infants. For example, gestation was used as a stratum to ensure that selection did not skew toward either newborns of a lower or higher gestational age. Exploratory outcome analyses used the same methods for binary outcomes and a linear model for normally distributed continuous outcomes. No adjustment was made for multiple testing.

Prespecified subgroup analyses were conducted based on consent type, gestational age, antenatal steroid exposure, and sex. Subgroup models included an interaction term and models were run for each subgroup. A sensitivity analysis included all randomized infants, including stillbirths. An analysis that included multiple imputation of missing data for the primary end point and its components was conducted using fully conditional specification logistic regression. Two-sided $P < .05$ was the threshold for statistical significance. Analyses were 2 sided and were conducted using SAS version 9.4 TS level 1M3 (SAS Institute).

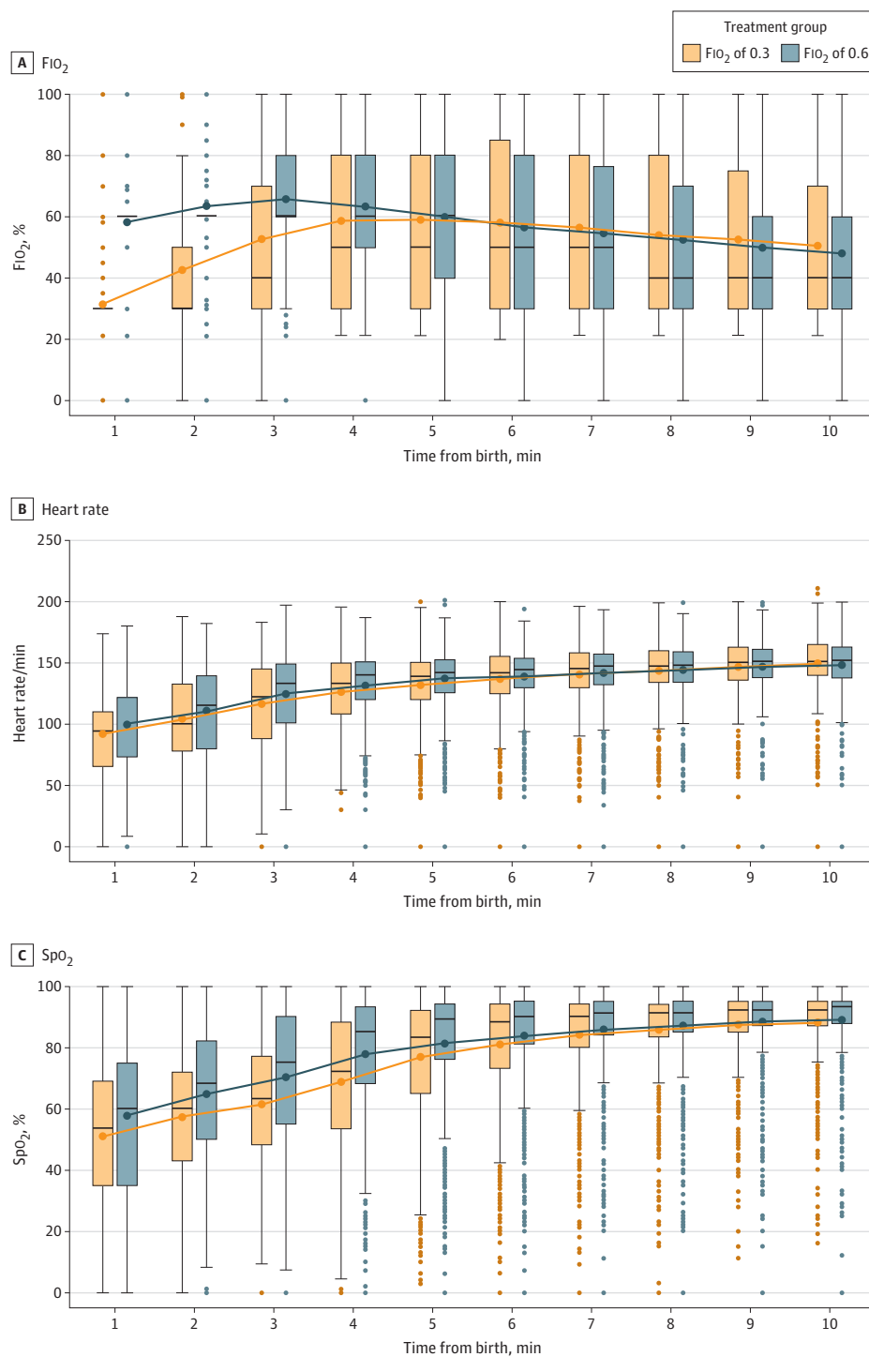
Results

Trial Population

Randomization occurred from September 2018 to September 2024. Of the 1641 newborns randomized, 827 were assigned to receive FiO₂ of 0.6, of whom 99 (12%) were excluded, and 814 were assigned to receive FiO₂ of 0.3, of whom 73 (9%) were excluded ([Figure 1](#)). A total of 1469 newborns were eligible and randomized, including 728 randomized to receive FiO₂ of 0.6 and 741 to receive FiO₂ of 0.3.

Most newborns were singletons (75%) and born in Australia (73%); 58% were cesarean delivery and 97% had some antenatal steroid exposure. Baseline maternal and newborn characteristics were balanced ([Table 1](#); [eTable 1 in Supplement 3](#)). Of families approached, 18% did not consent to inclusion of secondary and exploratory outcome data. The randomized intervention was received by 94% of newborns. Overall, 575 newborns (39%) (38% in the FiO₂ of 0.6 group and 41% in the FiO₂ of 0.3 group) required escalation to FiO₂ of 1.0 due to inadequate clinical response. Twenty newborns (1%) died in the delivery room. There were no adverse events attributed to the intervention.

Figure 2. Fraction of Inspired Oxygen (F_{iO_2}), Oxygen Saturation (SpO_2), and Heart Rate Over the First 10 Minutes



Primary and Secondary Outcomes

The primary outcome was ascertained in 96.9% of newborns included in the primary analysis and missing in 25 (3.4%) of those assigned to F_{iO_2} of 0.6 and 21 (2.8%) of those assigned to F_{iO_2} of 0.3. Neuroimaging was performed in 96% of newborns. There was no difference in the primary outcome

of death or major brain injury by 36 weeks' gestational age between those randomized to receive F_{iO_2} of 0.6 vs 0.3 (330 of 703 [46.9%] vs 344 of 720 [47.8%]; relative risk, 0.98 [95% CI, 0.89-1.09]) (Table 2).

A total of 229 newborns (16%) died by 36 weeks' gestation, most commonly due to cardiorespiratory failure (87 [37%])

Table 3. Newborn Status in the Delivery Room and on Admission to the NICU

	No. (%)	
	FiO ₂ of 0.6 (n = 728)	FiO ₂ of 0.3 (n = 741)
Delivery room outcomes		
FiO ₂ increase to 1.0	277 (38)	298 (41)
Intubated	281 (47)	313 (52)
Received chest compressions	11 (2)	30 (5)
Received epinephrine	4 (1)	14 (2)
Time to cord clamping, median (IQR), s	45 (10-60) [n = 568]	32.5 (10-60) [n = 582]
Apgar score at 5 min <7	112 (19)	153 (25)
SpO ₂ at 5 min		
<80%	190 (29)	282 (42)
≥80%	379/659 (58)	294/669 (44)
80%-85%	72/659 (11)	72/669 (11)
≥95%	117/659 (18)	86/669 (13)
Time to first breath, median (IQR), s	1.0 (0.0-1.0) [n = 667]	1.0 (0.0-2.0) [n = 684]
Starting SpO ₂ , mean (SD)	57.9 (24.3) [n = 307]	51.2 (25.1) [n = 312]
Ventilatory status on NICU admission ^a		
Any surfactant	246 (42)	262 (43)
Intermittent mandatory ventilation	247 (42)	279 (46)
Continuous positive airway pressure	339 (57)	325 (53)
High frequency ventilation	11 (2)	9 (1)
Inhaled nitric oxide	1 (<0.1)	2 (<0.1)
High flow oxygen	3 (1)	3 (<0.1)
Other modes of ventilation	13 (2)	16 (3)

Abbreviations: FiO₂, fraction of inspired oxygen; NICU, neonatal intensive care unit; SpO₂, oxygen saturation as measured by pulse oximetry.

^a Ventilatory support on admission to the NICU. Modes of ventilation are mutually exclusive.

in the FiO₂ of 0.6 group vs 46 [39%] in the FiO₂ of 0.3 group; eTable 2 in Supplement 3). Rates of brain injury (281 [42.4%] in the FiO₂ of 0.6 group vs 290 [43.2%] in the FiO₂ of 0.3 group; RR, 0.99 [95% CI, 0.87-1.11]) and death (112 [15.4%] in the FiO₂ of 0.6 group vs 117 [15.8%] in the FiO₂ of 0.3 group; RR, 1.00 [95% CI, 0.79-1.27]) by 36 weeks' gestation were similar (Table 2).

Sensitivity analyses including stillbirths did not change findings (eTable 3 in Supplement 3). Predefined subgroup sensitivity analyses by gestational age, whether consent waiver was used, exposure to any antenatal steroids, and sex also showed no difference in the primary outcome between intervention groups (eTable 4 in Supplement 3).

Exploratory Outcomes

Figure 2 illustrates the changes in SpO₂, FiO₂, and heart rate over the first 10 minutes of life and until admission into the NICU. Area under the curve analyses showed that SpO₂, FiO₂, and heart rate were higher in newborns assigned to receive initial FiO₂ of 0.6 for the first 5 and 10 minutes from birth (eTable 5 in Supplement 3).

Newborns in the FiO₂ of 0.6 group, compared with the FiO₂ of 0.3 group, were less likely to receive chest compressions (2% vs 5%) or epinephrine (1% vs 2%) and more likely to reach SpO₂ > 80% by 5 minutes (58% v 44%) (Table 3) and had higher initial SpO₂ (Table 3). There were no differences in time to first spontaneous breath or respiratory management on admission to the NICU (Table 3).

Infants assigned to the FiO₂ of 0.6 group had higher rates of ventriculomegaly (6.4% vs 2.4%; *P* = .004), but no group differences were observed in rates of other types of brain injury including intraventricular hemorrhage grades 3 and 4 and periventricular leukomalacia (Table 2).

Discussion

This study is the largest randomized clinical trial to the authors' knowledge to compare delivery room resuscitation of very preterm infants with a higher (FiO₂ of 0.6) vs lower (FiO₂ of 0.3) initial oxygen concentration. No differences were found between the groups in the composite outcome of death or brain injury at 36 weeks' gestational age.

The absence of a difference in the primary outcome could be due to several factors. First, the separation in FiO₂ between the groups may not have been large enough to produce measurable clinical differences in major outcomes such as death or brain injury. For example, almost the same percentage of infants required escalation of FiO₂ to 1.0. However, FiO₂ limits were chosen to reflect current guidance⁹—to start with FiO₂ of 0.3 and not exceed FiO₂ of 0.6—which was important for the consent waiver process and because meta-analyses had shown that resuscitating with FiO₂ less than or equal to 0.3 vs greater than or equal to 0.6 produced measurable differences in physiological parameters and early clinical outcomes.²⁰ Nevertheless, as this trial showed, detecting

differences in long-term clinical outcomes with these parameters may require trials with larger sample sizes.

Although the primary outcome did not differ between groups, the trial provides important insights into early physiological responses and the potential implications of initial oxygen strategy. Infants assigned to receive initial FIO_2 of 0.6 were more likely to achieve target preductal SpO_2 and heart rate greater than 100/minute by 5 minutes—2 critical early indicators associated with lower risk of severe intraventricular hemorrhage and death.²¹ They also had fewer episodes of hypoxia and bradycardia and required fewer intensive resuscitation interventions, such as chest compressions and epinephrine, compared with infants receiving initial FIO_2 of 0.3. These differences suggest improved physiological stability in the FIO_2 of 0.6 group during the first minutes of life. Failure to achieve SpO_2 of at least 80% by 5 minutes is consistently associated with increased risks of death and brain injury in preterm infants.²²

In 2025, the International Liaison Committee on Resuscitation removed previous caution against using FIO_2 of 1.0 for full-term infant resuscitation, recognizing that previous research did not blend or adjust FIO_2 to target SpO_2 . For preterm infants, the International Liaison Committee on Resuscitation has now called for more research on optimal starting FIO_2 values but, until that is available, suggests that clinicians adjust FIO_2 to target SpO_2 of 80% to 85% by 5 minutes while keeping heart rate greater than 100/minute.²³

The strengths of this study include its relatively large sample size, high fidelity to randomized interventions, and high ascertainment of the primary outcome.²⁴ Notably, a large

percentage of infants were enrolled under consent waiver, which increased generalizability by allowing for unbiased inclusion of all eligible infants regardless of clinical urgency—a key challenge in delivery room trials.²⁴

Limitations

This trial has limitations. First, it did not include FIO_2 of 0.4, which is frequently used in clinical practice,¹² nor did it examine higher starting doses such as FIO_2 of 1.0. Second, it was not powered to assess the impact of other concurrent delivery room interventions that can significantly influence oxygenation, such as delayed cord clamping, positive end-expiratory pressure strategies, or the use of different respiratory devices.²⁴⁻²⁶

Conclusions

This trial found no difference in survival without brain injury at 36 weeks' corrected gestational age when respiratory support at birth was initiated with FIO_2 of 0.6 vs FIO_2 of 0.3, followed by titration to standard SpO_2 targets. Although infants initially receiving FIO_2 of 0.6 were less likely to experience early hypoxemia, bradycardia, or require advanced resuscitation, these findings were not accompanied by improvements in major neonatal outcomes, underscoring the continuing uncertainty about the optimal initial oxygen concentration. These findings lay a foundation for future trials to determine whether different initial FIO_2 strategies—potentially including FIO_2 of 1.0—can improve survival and long-term outcomes.

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