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Targeted oxygenation in the respiratory care of premature infants at delivery—effects on outcome: a randomised controlled trial (Torpido 3060) study protocol

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ABSTRACT

Introduction The safest oxygen levels needed for preterm infant respiratory support at birth are uncertain. We aimed to compare the outcomes of infants up to 28[6] weeks gestation who had respiratory care initiated at birth with fractional inspired oxygen (FiO_2) 0.3 or 0.6, which was adjusted to meet specific oxygen saturations (SpO_2).

Methods This randomised controlled phase III trial was stratified by (1) site, (2) gestation and (3) multiplicity. Infants between 23+0 to 28+6 weeks gestation were randomised to initial respiratory support with FiO_2 0.3 or 0.6, adjusted to meet common SpO_2 targets for the first 10 min.

Primary outcome Survival to 36 weeks gestation without documented brain injury.

Assessments FiO_2, SpO_2 and heart rate were recorded each minute from delivery for 10 min. Assessments were obtained at baseline, 36 weeks, discharge and at 2 years corrected gestation, along with a parent questionnaire.

Statistical analysis plan Assuming 32% of infants would die or survive with brain injury by 36 weeks, 735 infants per arm (1470 total) were needed to detect a risk difference of 8% (25% relative risk reduction), with 10% non-adherence to protocol, 85% β and 5% α.

Ethics Approved by the John Hunter Human Research Ethics Committee (2019/ETH/3837) for waiver of consent for all Australian sites for randomised allocation and primary outcome.

Conclusion Recruitment started in 2018 and was achieved on 30 September 2024. The Data and Safety Committee review found no major safety concerns at 50% recruitment.

Trial registration number ACTRN 12618000879268.

WHAT IS ALREADY KNOWN ON THIS TOPIC?

⇒ The safest level of oxygen for initiating respiratory support of preterm infants at birth is unknown.

WHAT THIS STUDY HOPES TO ADD?

⇒ This is the largest (n=1470) randomised trial to determine whether lower (fractional inspired oxygen, FiO_2, 0.3) or higher (FiO_2 0.6) initial oxygen levels decreases risk of death or brain injury by 36 weeks gestation in very preterm infants.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The results of this study will guide oxygen treatment of preterm infants at birth, inform on international guidelines and practice and springboard future research for other understudied populations, such as moderate to late preterm infants.

INTRODUCTION

The safest level of oxygen for initiating respiratory support of preterm infants (<37 weeks gestation) at birth is unknown. Five randomised controlled trials (RCTs) and five quasi-RCTs of 2164 infants suggest that using room air (fractional inspired oxygen (FiO_2) 0.21) instead of pure oxygen (FiO_2 1.0) to initiate delivery room resuscitation for full-term hypoxic infants reduced short-term mortality (typical risk ratio (RR) 0.73; 95% CI (CI): 0.57 to 0.94).[1]

Preterm infants, however, have immature lungs and may require supplemental oxygen to prevent hypoxaemia. They also have less antioxidant protection[2] that places them at an increased risk of oxidative stress and injury.[3] International guidance for oxygen treatment of preterm infants at birth changed from 2006[4] to recommend the use of lower levels of oxygen (FiO_2 0.21–0.3) to initiate respiratory support in the delivery room[5] in order to avoid oxidative stress and injury.

In 2017, the largest RCT to examine the impact of lower or higher initial FiO_2

for initial respiratory support of 292 preterm infants below 32 weeks gestation (Targeted Oxygen for Respiratory Support of Preterm Infants and their Developmental Outcomes trial (To2rpido), Australian and New Zealand Clinical Trials Network Registry (ACTRN 12610001059055) and National Malaysian Research Registry (NMRR-07-685-957)) showed that initial oxygen levels did not impact mortality or common neonatal morbidities such as bronchopulmonary dysplasia (BPD). A post hoc analysis, however, found an increased risk of death (RR 3.9 (95% CI 1.1 to 13.4); p=0.01) in infants <28 weeks gestation if respiratory support was initiated with FiO_2 0.21 instead of 1.0.[6]

Due to loss of equipoise for using high (FiO_2>0.65) levels of initial oxygen in the delivery room,[7 8] To2rpido was unable to achieve its target sample size of 1976 infants. Subsequently, an individual meta-analysis of individual patient data from eight RCTs conducted between 2006 to 2013, including To2rpido, found no difference in the association between initial FiO_2 and mortality and morbidity,[9] but that the risk of death and intraventricular haemorrhage was increased if infants did not reach minimum oxygen saturations (SpO_2) of 80% by 5 min.[10]

Recently, the Netmotion study conducted a network meta-analysis of 12 RCTs and showed, with low certainty, that resuscitation with high (≥0.90) initial FiO_2 was associated with significantly reduced mortality compared with low (≤0.3) (OR 0.45, 95% credible interval (CrI) 0.23–0.86) and intermediate (0.5–0.65) FiO_2 (OR 0.34, CrI 0.11–0.99) oxygen levels.[11] Whether preterm infants need higher oxygen levels at birth than term infants is uncertain, but Dekker *et al* found that hypoxia depressed preterm infant breathing effort at birth.[12]

The primary objective of the Torpido 3060 study was thus to determine whether respiratory support with higher or lower levels of FiO_2 at birth changed the risk of survival with brain injury. This report summarises Study Protocol V.1.4, dated 16 April 2021 (online supplemental appendix 1). The trial is registered with the Australian and New Zealand Clinical Trials Registry (ACTRN 12618000879268; 25 May 2018).

METHODS

Objective

We aimed to compare short- and long-term outcomes of preterm infants from 23+0 to 28+6 weeks gestation who have had respiratory support at birth initiated with either FiO_2 of 0.3 or 0.6.

Hypothesis

Initiating respiratory support of preterm infants<29 weeks gestation with higher initial FiO_2 will improve survival without brain injury by 36 weeks corrected gestation.

Primary outcome

Survival to 36 weeks gestation without documented brain injury, determined by neuroimaging and reported by a blinded radiologist. Brain injury is defined as any intraventricular haemorrhage grades 3 or 4, echo-dense intraparenchymal lesions (bright lesions indicative of possible previous ischaemia), periventricular leukomalacia or porencephalic cysts.

Secondary outcomes

1. All-cause mortality until hospital discharge.
2. Major brain injury until at 36 weeks gestation.

Tertiary (hypothesis-generating) outcomes

1. SpO_2 < or ≥80% by 5 min of life.
2. Time to reach SpO_2≥80%.
3. Heart rate (HR)<100 beats per minute (bpm) or ≥100 bpm at 5 min of age.
4. Intubation in delivery suite.
5. Apgar at 1 and 5 min.
6. Morbidities: (a) BPD defined as survival to 36 weeks and requirement for supplemental oxygen or respiratory support; (b) retinopathy of prematurity (ROP) defined as stage 3 or 4 ROP and/or requiring surgical or medical intervention[13] ; (c) necrotising enterocolitis associated with surgery or death, measured to hospital discharge; (d) late-onset sepsis with a culture positive body fluid and (e) patent ductus arteriosus requiring medical or surgical treatment.
7. Duration of hospitalisation.
8. Survival without major disability at 2–3 years corrected for gestation, assessed with either the Bayley Scales of Infant Development III and after 2021, V. IV and/or the Ages and Stages Questionnaire and a Short Health Status Questionnaire.

Trial design

A phase III, randomised, two parallel-arms trial. Treatment allocation was balanced using minimisation techniques for study site, gestation (</≥ 26 weeks gestation) and multiple births.

Study setting

Maternity hospitals with a tertiary-level Neonatal Intensive Care Unit (NICU) that are able to provide care to infants from at least 24 weeks gestation

Population criteria

Inclusion criteria: infants born between 23+0 and 28+6 weeks gestation needing respiratory support at birth (clinically determined). Exclusion criteria: major cardiopulmonary abnormalities affecting oxygenation and/or congenital malformations affecting neurodevelopment and survival.

Timeline

See table 1.

Randomisation

Randomisation was conducted through Flexitrials (www.flexetrials.com.au) before birth and when delivery was

Table 1 Timeline for patient participation

	Before delivery	Post delivery	36 weeks	Discharge	Follow-up* (months)			
					6	12	18	24
Opt-In to follow-up		X						
Randomisation	X							
Serious Unexpected Serious Adverse Reactions†		X	X	X				
Clinical data	X	X	X	X				
Outcome events		X	X	X				X
Record/confirm contacts for family*				X	X	X	X	X
Ages and Stages Questionnaire								X
Bayley Scale of Infant Development assessment‡								X

*Contact details and follow-up only when consent is provided.
†Serious Unexpected Serious Adverse Reactions will be collected up to 30 days after the intervention.
‡Bayley Scale of Infant Development where consistent with routine practice at the participating site.

considered inevitable. Each participant was assigned a study number and a treatment arm. Written confirmation of successful randomisation was provided to the site and site principal investigator.

Consent process

Three consent processes were used depending on local ethics regulations. All Australian sites were recruited under a consent waiver process for randomised allocation and the primary outcome. Other sites used consent waiver, deferred or prospective consent. Consent documents are included in online supplemental appendixs 2 and 3.

Rationale for consent waiver

Recruiting representative and sufficiently large populations into resuscitation studies is difficult if prospective informed consent is used.[6] Consent waiver for resuscitation studies is strongly supported by parents as a means to acquire clinically important knowledge.[14] The two treatment arms in this study were within the range recommended by international[5] guidelines as being acceptable, and less likely to cause hypoxia or hyperoxemia than FiO_2 0.21 or 1.0.[1] The study was approved by the John Hunter Human Research Ethics Committee (2019/ETH/3837) for waiver of consent in all Australian sites for randomised allocation and primary outcome. Informed consent was obtained as an opt-in for secondary outcome data (online supplemental appendixs 1 and 2).

Patient and public involvement

The research question and outcome measures were informed by consultation with Miracle Babies, a not-for-profit organisation of parents and preterm infants in Australia.[15] Co-author MC, a parent of three preterm infants, was involved in the development of the study, including the application for consent waiver. There was minimal burden for patients in regards to either intervention or outcome measures as these were part of standard care.

Interventions

Randomised infants who were born alive and considered eligible for active management were placed on the resuscitation bed. Care was initiated according to local practice, including achieving lung expansion with Continuous Positive Airway Pressure (CPAP) or ventilation. A pulse oximeter sensor was placed on the right wrist *before connecting to the pulse oximeter* to decrease time to accurate reading.[16] Initial FiO_2 was set using an oxygen blender at 0.6 or 0.3, as randomised.

Oxygen saturation (SpO_2) targets

The aim was to reach SpO_2 80–85% by 5 min and 85–95% by 10 min. Clinicians were recommended to keep the initial level of FiO_2 (at 0.3 or 0.6) for at least 5 min, unless HR was <100 bpm and not rising, or SpO_2 was >95%. FiO_2 could then be adjusted by 0.1–0.2 aliquots every 30–60 s to achieve target SpO_2 until admission to NICU.

Time 0 of life was defined as delivery of the infant body. The procedures for delayed cord clamping were recorded: yes/no and duration.

Transport to the NICU

This occurred when the infant was clinically stable (eg, SpO_2 between 85% and 95% and HR >100 bpm). FiO_2 was adjusted to maintain SpO_2 between 85% and 95% during transfer. Subsequent care after admission to the NICU was at the discretion of clinical team.

Blinding

Parents were blinded to study intervention arm, but staff in the delivery room were not blinded as FiO_2 had to be adjusted to meet SpO_2 targets. Equipment (blenders and oxygen analysers) were visible to the clinicians.

Variations

FiO_2 could be increased immediately to 1.0 if an infant required external cardiac massage or resuscitation medications.

Adverse events (AEs) were defined as any untoward medical occurrence in a patient which did not necessarily have a causal relationship with trial intervention. AEs were not required to be reported.

A Suspected Unexpected Serious Adverse Reaction (SUSAR) was an adverse unexpected event that was related to the intervention. SUSARs were required to be reported by the site investigator to the Clinical Trials Centre (CTC), Trial Management Committee (TMC) and institutional review board within 30 days and would be reviewed by the Independent Data and Safety Monitoring Committee (IDSMC).

Sample size and power calculation

A total of 735 infants per arm (1470 total) was required to provide 85% power, at two-sided 5% significance level, to detect an absolute risk difference of 32% versus 24% (ie, 25% a relative risk reduction) in the primary endpoint (brain injury free survival to 36 weeks) while allowing for 10% non-adherence to assigned protocol treatment. Multiple babies from the same birth were randomised to the same treatment arm. An intracluster correlation of 0.3 and an average cluster size of 1.15 were assumed, and the sample size was adjusted accordingly. The sample size was based on current and conservative assumptions about event rates and compliance. Parameters were reviewed at the interim analysis and were unchanged at the completion of the study.

Statistical analysis plan

Summary statistics (means and SD, medians and quartiles) will be presented for continuous baseline variables. Categorical outcomes will be summarised by the proportion of subjects falling into each category. Analysis of effectiveness will be conducted according to the intention-to-treat principle. The level of significance for the study is 5% (two-sided). There will be no adjustment for multiple comparisons. Descriptive statistics of baseline demographic and clinical variables will be summarised by allocated treatment groups using appropriate summary measures.

Comparisons between randomised groups adjusting for stratification factors will use repeated-measures analysis to account for multiple births. Analysis of binary outcomes will use linear models with a log link, the treatment difference being reported as an RR and 95% CI. If the counts for tertiary outcomes are small, then the analysis may not be adjusted for the stratification factors. Normally distributed continuous variables will be analysed using linear models, with the treatment difference being reported as a mean difference and CI. The distribution of other outcomes will be assessed, and the appropriate analysis ascertained. Analyses adjusting for other baseline covariates will be explored using similar methods. Subgroup analyses will be prespecified.

Primary outcome analysis

The primary outcome of death or brain injury will be analysed with a linear model with a log link, adjusting for stratification factors and multiple births. The results will be summarised with the number and percentage of events and the intervention comparison summarised with a relative risk and 95% CI.

Secondary and tertiary outcomes

The secondary outcomes will use the same analysis principles as the primary outcome. Tertiary (hypothesis-generating) outcomes will use the same methods for binary outcomes and a linear model adjusting for the stratification factors and accounting for multiple births for normally distributed continuous outcomes.

Interim analyses

The TMC monitored site protocol adherence and compliance and accrual rate. The Data and Safety Management Committee (DSMC) reviewed interim data and emerging evidence from other studies after 50% of the projected total number of participants for the primary endpoint and then yearly or more frequently if required. There were no protocol changes prior to the first DSMC review.

Prespecified subgroups

The primary outcome will be analysed in each of the prespecified subgroups (consent type, gestation, steroid treatment, gender). A model including the intervention, the subgroup and the intervention by subgroup interaction will be run, as well as models for each level of the subgroup separately. Sensitivity analyses will be conducted for infants not requiring respiratory support at birth.

Study coordination

This was overseen by the NHMRC CTC at the University of Sydney, Sydney, NSW, Australia.

Independent Data and Safety Monitoring Committee

The IDSMC was blinded to treatment arm unless a review of non-blinded data was required. The IDSMC provided independent assessment of patient safety and trial progress and made recommendations to the TMC about the continuation of the trial based on data made available by the trial statistician. Agreed terms of reference for the IDSMC incorporating appropriate statistical methods for considering early stopping of the trial (eg, Haybittle-Peto criteria)[17] were developed with the TMC (supplement, online supplemental appendix 4).

Ethics and regulatory compliance

This study was conducted according to the Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) annotated with TGA comments (July 2000), the NHMRC Statement on Ethical Conduct in Research Involving Humans (Commonwealth of Australia 2007) and the NHMRC Australian Code for the Responsible Conduct of Research (Australian Government 2007). No patient was

recruited to the study until all the necessary approvals had been obtained.

Confidentiality

Data generated by this study remain confidential, stored securely at the NHMRC CTC, University of Sydney, and will only be available to people directly involved with the study and/or who have signed a Confidentiality Agreement. Personal data identifying trial subjects will be held securely at the CTC for the purpose of follow-up if the patient is unable to/wishes to discontinue participation.

Protocol amendments

Changes and amendments to the protocol and consent forms could only be made by the TMC and if approved by the institutional IRB.

Data handling and record keeping

All trial data required for the monitoring and analysis of the study were recorded on electronic case record forms (eCRFs). Data corrections were done according to instructions and the investigator was asked to confirm the accuracy of completed CRFs by signing key CRFs as indicated. Source documents pertaining to the trial (eg, subject's medical records, hospital charts, diagnostic tests) remained at the site. Information for the eCRF included subject details, dates of consent, any AEs and dates of entry and exit from the study. All study-related documentation at Australian sites will be maintained for at least 15 years following the completion of the study and other sites as per national guidelines.

Study monitoring

Data from this study were monitored by Clinical Trials Program staff from the CTC and included centralised review of CRFs and other study documents for protocol compliance, data accuracy and completeness. Signing the informed consent form allowed CTC staff direct access to their medical records and the study data. If consent was declined, CTC were only given access to de-identified information about routine hospital assessments.

Audit and inspection

This study may be subject to audit or inspection by representatives of the CTC or representatives of regulatory bodies (eg, Therapeutic Goods Administration).

Publication policy

The first publication will be the protocol, followed by the report of the full trial results. Subsequent publications of data subsets will be conducted if required. The TMC will review and approve all publications according to a publication plan which includes authorship, target journals and expected dates of publication.

CONCLUSION

Based on trials on term infants[1] and concerns about oxidative stress, air and lower oxygen concentrations have been used to initiate respiratory support of preterm infants for more than 15 years but emerging information suggests that lower oxygen concentrations may be associated with poorer outcomes.[10] The amount of oxygen provided to an infant in the first few minutes of life may impact on short- and long-term outcomes and without answering this question, more than 1 million very preterm infants are at risk of potentially avoidable harm.

The Torpido 3060 represents the largest RCT of its kind to date and will also provide, together with the HiLO study (NCT 03825835), information from four consent processes: waiver, deferred and prospective informed. Collectively, the Torpido 3060 and HiLo studies will contribute to a prospective metanalysis[18] that has the potential to change worldwide practice, including optimum SpO_2 trajectories in the first minutes after birth, and the relationship between oxygenation at birth and longer-term outcomes including neurodevelopment.

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Contributors All authors are responsible for approving any manuscripts for presentation and publication. JLO (guarantor) is the principal investigator, co-chair of the TMC, site investigator for the Royal Hospital for Women, conceived study idea, obtained study funding, led study organisation, recruitment and presentation of the data. JT assisted with ethics approval, was site investigator for the John Hunter Children's Hospital and is a member of the TMC. AK is the principal statistician, responsible for the statistical analysis plan and statistical analysis and is a member of the TMC. IM is the lead statistician of the NHMRC Clinical Trial Centre and member of the IDSMC, and will assist AK in the statistical analysis. CY is the principal study coordinator. MC is the parent representative and assisted with ethics approval and is a member of the TMC. IW was the site investigator for John Hunter Children's Hospital, is a member of the TMC and contributed to study design. WH (retired) is a member of the TMC and contributed to the study design. PD is a member of the TMC and contributed to the study design. AG is project manager at the NHMRC Clinical Trial Centre and was responsible for site coordination with CY. JS was the director of the NHMRC Clinical Trial Centre, is a member of the TMC and contributed to the study design. AK was assistant director of the NHMRC Clinical Trial Centre, is a member of the TMC and contributed to the study design. KL is a member of the TMC and contributed to the study design. DO is site investigator for the Royal Prince Alfred Hospital, is a member of the TMC and contributed to the study design. WTM is director of Perinatal Trials at the NHMRC Clinical Trial Centre, is co-chair of the TMC and was responsible with JLO for obtaining funding and ethics approval in Australia.

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Competing interests JLO received honoraria from Mallinkrodt Inc for travel, research and presentations. No other has any known conflict of interest.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Consent obtained from parent(s)/guardian(s).

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REFERENCES

1 Welsford M, Nishiyama C, Shortt C, *et al*. Room Air for Initiating Term Newborn Resuscitation: A Systematic Review With Meta-analysis. *Pediatrics* 2019;143:e20181825.
2 Kicinski P, Malachowska B, Wyka K, *et al*. The level of extracellular superoxide dismutase in the first week of life in very and extremely low birth weight infants and the risk of developing bronchopulmonary dysplasia. *J Perinat Med* 2019;47:671–6.
3 Tataranno ML, Oei JL, Perrone S, *et al*. Resuscitating preterm infants with 100% oxygen is associated with higher oxidative stress than room air. *Acta Paediatr* 2015;104:759–65.
4 American Heart Association, American Academy of Pediatrics. 2005 American Heart Association (AHA) Guidelines for Cardiopulmonary Resuscitation (CPR) and Emergency Cardiovascular Care (ECC) of Pediatric and Neonatal Patients: Neonatal Resuscitation Guidelines. *Pediatrics* 2006;117:e1029–38.
5 Perlman JM, Wyllie J, Kattwinkel J, *et al*. Part 11: Neonatal resuscitation: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation* 2010;122:S516–38.
6 Oei JL, Saugstad OD, Lui K, *et al*. Targeted Oxygen in the Resuscitation of Preterm Infants, a Randomized Clinical Trial. *Pediatrics* 2017;139:e20161452.
7 Clark RL, Lui K, Oei JL. Use of oxygen in the resuscitation of preterm infants: current opinion and practice in Australia and New Zealand. *J Paediatr Child Health* 2009;45:31–5.
8 Oei JL, Ghadge A, Coates E, *et al*. Clinicians in 25 countries prefer to use lower levels of oxygen to resuscitate preterm infants at birth. *Acta Paediatr* 2016;105:1061–6.
9 Oei JL, Vento M, Rabi Y, *et al*. Higher or lower oxygen for delivery room resuscitation of preterm infants below 28 completed weeks gestation: a meta-analysis. *Arch Dis Child Fetal Neonatal Ed* 2017;102:F24–30.
10 Oei JL, Finer NN, Saugstad OD, *et al*. Outcomes of oxygen saturation targeting during delivery room stabilisation of preterm infants. *Arch Dis Child Fetal Neonatal Ed* 2018;103:F446–54.
11 Sotiropoulos JX, Oei JL, Schmölzer GM, *et al*. Initial Oxygen Concentration for the Resuscitation of Infants Born at Less Than 32 Weeks' Gestation: A Systematic Review and Individual Participant Data Network Meta-Analysis. *JAMA Pediatr* 2024;178:774–83.
12 Dekker J, Martherus T, Lopriore E, *et al*. The Effect of Initial High vs. Low FiO_2 on Breathing Effort in Preterm Infants at Birth: A Randomized Controlled Trial. *Front Pediatr* 2019;7:504.
13 Hellström A, Smith LEH, Dammann O. Retinopathy of prematurity. *Lancet* 2013;382:1445–57.
14 Rich WD, Katheria AC. Waiver of Consent in a Trial Intervention Occurring at Birth-How Do Parents Feel? *Front Pediatr* 2017;5:56.
15 Miracle Babies. Available: www.miraclebabies.org.au [Accessed 22 Jan 2025].
16 O'Donnell CPF, Kamlin COF, Davis PG, *et al*. Obtaining pulse oximetry data in neonates: a randomised crossover study of sensor application techniques. *Arch Dis Child Fetal Neonatal Ed* 2005;90:F84–5.
17 Blenkinsop A, Parmar MK, Choodari-Oskooei B. Assessing the impact of efficacy stopping rules on the error rates under the multi-arm multi-stage framework. *Clin Trials* 2019;16:132–41.
18 Sotiropoulos JX, Schmölzer GM, Oei JL, *et al*. PROspective Meta-analysis Of Trials of Initial Oxygen in preterm Newborns (PROMOTION): Protocol for a systematic review and prospective meta-analysis with individual participant data on initial oxygen concentration for resuscitation of preterm infants. *Acta Paediatr* 2023;112:372–82.